VOLUME 77 • MARCH 1957 • NUMBER 3

# A.M.A. ARCHIVES OF NEUROLOGY & PSYCHIATRY


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The "March" of Temporal Lobe Epilepsy
*Janice R. Stevens*

Asynchronism of Electrical Activity of Frontal Lobes During Sleep
*C. L. Adams, E. L. Gibbs, and F. A. Gibbs*

Chlorpromazine (Thorazine) Treatment of Disturbed Epileptic Patients
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The Pattern of Conduction of Amygdaloid Seizure Discharge
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*Marian W. Kies, Dale Horst, Edward V. Evarts, and Norman P. Goldstein*

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Dr. John C. Eccles is Professor of Physiology at the Australian National University, Canberra. His previous books include *Reflex Activity of the Spinal Cord*, and *Neurophysiological Basis of Mind*. The present book grew out of the 1955 Herter Lectures, given by the author at The Johns Hopkins University School of Medicine.

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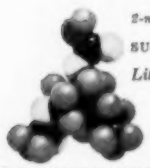

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# The "March" of Temporal Lobe Epilepsy

JANICE R. STEVENS, M.D., Portland, Ore.

"I doubt not that there is some order throughout, from the warning to the end of the post paroxysmal stage."[1]

With these words John Hughlings Jackson, in 1880, discussed the results of his exhaustive clinical studies of epileptic patients whose symptoms comprised a number or a series of consecutive or simultaneous alterations of thought, emotion, sensation, and behavior. Thus he indicated his confidence that the varied manifestations of each epileptic attack, whether "dreamy state," uncinate fit, hallucination, or complex automatism, were consistent within the framework of the attack, if only the framework itself could be discerned.

The present study is a direct outgrowth of lengthy clinical and electroencephalographic investigation carried out on a group of epileptic patients in collaboration with Drs. Paul MacLean and Gilbert Glaser.[2] In the course of these studies, we were repeatedly struck by the frequency of association of certain groups of symptoms within the boundaries of a single repeated epileptic seizure. The characteristic association of certain emotional, psychic, and physical states in a group of epileptic attacks electroencephalographically originating in the region of the temporal lobes posed the problem of whether or not careful analysis of the sequential pattern of epileptic attacks originating in this area might give information as to the relationship of function and anatomy in the temporal region of the brain. By study of the chronological development of such attacks, it is possible that one can discover a characteristic "march" (or, more likely, a series of typical "marches") of symptoms and signs for the discharging temporal lobe and environs, comparable to the patterned march of seizure activity originating in the primary sensory and motor areas.

Persons suffering from psychosensory and psychomotor epilepsy offer a unique opportunity for exploration of the functional anatomical relationships of the temporal lobe. As is well known, it is only in such subjects that local electrical stimulation of the temporal cortex produces complex states of remembering, illusion, and hallucination.[3] It would appear, as Penfield and Rasmussen [4] have suggested, that artificial electrical stimuli applied to the "normal" cortex are incapable of evoking any but the crudest motor and sensory responses, the "in-born" responses. However, in the cortex "sensitized" by repeated trains of epileptic seizures, the electrical impulse may precipitate an attack of the greatest complexity, apparently following a "well worn path" characteristic of the patient's usual seizure pattern.[5]

The electrical origin of complex psychomotor and psychosensory attacks is peculiarly limited to the temporal lobes and the immediately surrounding cortex. For this reason, the patient with "temporal lobe seizures" deserves particular and minute study

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From the Division of Neurology, University of Oregon Medical School.

of the sequential disposition of seizure pattern in order that our speculations as to functional relationships of the human temporal lobe may have a finite basis. Whether apparent functional relationships disclosed by the pattern of epileptic seizures in this region also obtain in the nonepileptic brain must, of course, remain in question.

## Material and Methods

In order to study the sequential relationships of psychomotor and psychosensory seizures, 40 patients have been chosen for seizure analysis, primarily because of their ability to describe lucidly a well-defined and consistent aura suggesting origin of seizures from the temporal and adjacent cortex. Descriptions of the motor component of seizures are available from reliable observers. None of these patients has a diagnosis of cerebral tumor or progressive degenerative disease of the central nervous system, and all are free of major neurological stigmata. Thirty-one of these patients demonstrated frank spiking or sharp activity at the temporal or basal region of the brain; six patients demonstrated focal slowing in the temporal region, and three patients repeatedly had normal electroencephalograms. All patients have had sleep encephalograms, and 15 had pentylenetetrazol (Metrazol) or photo-Metrazol activation. Half the group were studied in the clinics and laboratories of the Grace-New Haven Community Hospital and Yale University School of Medicine, and the other half are from the hospitals and clinics of the University of Oregon Medical School and the Veterans Administration Hospital in Portland, Ore.

The material presented is derived chiefly from repeated interviews with patients and their families. Interviews conducted while the patient was under the influence of amobarbital (Amytal) sodium were carried out in all cases, and additional information was elicited in this way in a number of instances. On the whole, it was found that information available readily under the influence of amobarbital sedation could usually be elicited following many interviews while the patient was without narcosis. The amobarbital interviews were of particular help in bringing out information embarrassing to the patient, such as the presence of visual and auditory hallucinations and the content of dreamy states. Interviews were structured toward elucidation of the chronological development of the seizure, as well as the nature of ictal experience. Immediate pre- and postictal behavior was also investigated but is not included in the present report.

## Results

Table 1 summarizes what appears to be the essence of content and sequence in each patient's attack. In order that the various patterns of temporal lobe seizures may be more readily appreciated, the major types of seizure manifestations have been grouped in separate tabulations identified by the characteristic common to the group. Patients may appear in more than one tabulation because of the presence of a variety of symptoms or signs which identify them with more than one subgroup.

This material suggests that there may indeed be an ordered arrangement of certain physical, psychic, and behavior patterns in the region of the temporal lobe. The multitude of symptomatic and behavioral states at first appears to defy rational organization, and one may well remember the warning of Sir William Gowers, who early in this century cautioned "that at the present state of our ignorance it seems more useful to gather facts than to formulate hypotheses."[6]

Although the above data by no means allow elaboration of a detailed homunculus of psychic or behavioral representation similar to what we have come to expect for sensorimotor representation from our Canadian colleagues, we may outline tentative and preliminary lines of form and pattern, subject, of course, to revision as our experience with this type of analysis widens.

Subjective experiences characteristic of the discharging temporal region appear to fall into four major groups:

1. Primary sensory receiving area for olfaction, taste, audition, and equilibrium.

2. Visceral sensation primarily related to the gastrointestinal tract, cardiorespiratory system, bladder, and deep body structures.

3. Complicated elaborations and distortions of the primary sensations.

4. A kaleidoscopic panorama of emotional and intellectual states, including fear, pleasure, sorrow, anger, anticipation, dread, sexuality, familiarity, strangeness, guilt,

TABLE 1.—*Summary of Content and Sequence of Individual Patient Attacks**

A. Gastric

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 RNP | Gastric | → | Fear; shivering; chills | → | Tension; bladder pressure | | | | | → | Searching; jumbled speech | → | G.S. | |
| 2 RT | Gastric | → | Fear | → | Bad Odor; visions | | | Threatening vision, death fear | → | Running; fight† or smoking | → | G.S. | | |
| 3 RNP | Gastric | → | Fear | → | Odor, bad | → | "Must go" | | → | Running; searching; fight† | → | G.S. | | |
| 4 BiF | Gastric | → | | → | Odor; taste | → | "Bad; done in" | | → | ..... | | ..... | | |
| 5 BiT | Gastric | → | Fear | → | Odor; taste | → | "Bad; nothing there" | | → | Gagging; choking; cyanosis | → | G.S. | | |
| 6 RNP | Gastric | → | Fear; indecision | → | Ears ring; hot & cold sensation | → | Wants to grab; wants to run | | → | Pallor; running; grabbing; snorting | → | ..... | | |
| 7 RAT | Heart frozen | → | Fear | → | | | Hallucination of dying; killing self with knife | | → | Beats chest | → | G.S. | | |
| 8 RNP | Gastric | → | Fear | → | Gagging; spitting up | → | Paranoid hallue. | | → | Shouts for help; vomits, wrings hands; automatic | | ..... | | |
| 9 NP | Gastric | → | | | | | | | | Gagging; choking; frothing | | | | |
| 10 RFT | Gastric | → | Insecurity | → | | → | "Can't go on" | | → | Speech arrest; staring; torsion | → | G.S. | | |
| 11 LAT | Bursting belly | → | Fear | → | Danger visions | | | | → | Inappropriate speech; hugs self | | | | |

B. Olfactory

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 RNP | Gastric | → | Fear | → | Foul smell and taste | → | | | Runs, searches; fights† | → | Smacking; drinking | → | G.S. | |
| 2 RT | Gastric | → | Fear | → | Bad smell | → | Threatening vision; death fear | → | Runs, shouts "help"; fights† | → | Smacking; chewing | → | G.S. | |
| 12 RT | Tinnitus; dizziness | → | Fear | → | Bad smell; tongue tingles | → | "Dizzy head" | → | Runs; fights† | → | Jerking, l. side | → | G.S. | |
| 13 RFT | | | Foreboding | → | Bad smell | → | | | | | Jerking, l. side | → | G.S. | |
| 14 NP | Dizziness; rocking | → | | | Bad smell; vision distorted | → | Sorrow; "want to cry" | → | Nausea; vomiting | → | Smacking; chewing; blinking | → | G.S. | |
| 15 RNP | Numb body, lips | → | "Far away" | | Bad smell; visions | → | Fear | → | | | | | G.S. | |
| 5 BiT | Gastric | → | Fear | | Odor; taste medicinal | → | "All gone"; "bad" | → | | | Gagging; choking | → | G.S. | |
| 16 BiF | Gastric | → | Anxiety | → | Peculiar odor; taste | → | "Bad"; "done in" | → | | | ..... | | ..... | |

TABLE 1.—*Summary of Content and Sequence of Individual Patient Attacks**
Continued

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | C. Tinnitus-Vertigo | | | | | | |
| 17 O | Whirling | → | "Outside it all" | → | V. & A. hallucinations; popular melody, crowds; "Why aren't I there?" | → | | | Repeats one word | → | G.S. |
| 18 RT | Dizziness | → | Unreality; strangeness | → | Pleasant familiar visions | → | | | Vomiting | → | G.S. |
| 19 LTy | Dizziness | → | Conscience bothers | → | | → | | | Chewing; smacking; drinking | → | G.S. |
| 20 NP | Dizziness; rocking | → | Vision distorted; bad smell | → | Sorrow; "want to cry" | → | Nausea; vomiting | → | Blinking; smacking; chewing | → | G.S. |
| 21 BIT | Humming | → | Strangeness; vision lost | → | "Sorry feeling"; "other world feeling" | → | | → | | | G.S. |
| 22 O | Humming | → | Auditory hallucinations | → | "Sorry feeling" for someone | → | | → | | | G.S. |
| 12 RT | Tinnitus; dizziness | → | Sound distorted | → | Fear | → | Bad smell, tongue tingles | → | Runs; fights† | → | G.S. |
| | | | | | D. Illusory States | | | | | | |
| 10 RFT | Vision; geometric figure | → | Unreality | → | Conscience bothers | → | | | Staring; speech arrest; torsion; fall | | |
| 23 LPT | Vision of totem; racing thoughts | → | Unreality | → | Dry throat; despair | → | Panic | → | Loss of speech, comprehension | | |
| 24 RAT | | | Familiarity; strangeness | → | Insecure; foreboding; morbid; depressed | → | Disaster, "can't go on" | → | Grab, run, shout, attack | → | G.S. |
| 25 LT | Thoughts race; "jackhammer" in head | → | "Out of world" | → | Want to be alone | → | Terror | → | Stamps, spits, runs; makes fists | → | G.S. |
| 18 RT | Humming | → | Strangeness | → | Vision decreased; hearing increased | → | World left behind | → | Fall | | |
| 26 RAT | Perfume smell | → | Unreality | → | Numb body, head | → | | | Fumbles with girls or self | → | G.S. |
| | | | | | E. Body | | | | | | |
| 15 RNP | Numb body, lips | → | "Far away" | → | Bad smell | → | Fear | → | | | G.S. |
| 27 RFTP | Electricity, whole body | → | Anger | → | Visions, animals chasing | → | Must grab, must run | → | Runs, shouts for help; attacks others | | |
| 28 RT | Body numb | → | Terrible pressure; thoughts congeal | → | Bursting inside | → | Eruption of laughing sensation | → | | | G.S. |
| 29 RPF | Crawling up spine | → | Dizziness; walls move | → | Visions, voices | → | | | Bewildered appearance; gibberish, nursery rhymes; slapping, snapping, and chasing | → | G.S. |

TABLE 1.—*Summary of Content and Sequence of Individual Patient Attacks**
Continued

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | F. Cephalic | | | | | |
| 11 LAT | Swelling head | → | Rush of crystal-clear thoughts; "all-important" | → | Pleasant visions | → | Inappropriate speech, stares; hugs self | | | |
| 1 RNP | Tingling, feet to head | → | Anticipation, good; feelings of familiarity and strangeness | → | Tension, bladder pressure | → | Searching; jumbled speech | → | G.S. | |
| 30 RNP | Tingling throat, mouth, head | → | Pleasant "career" feeling | → | | → | Coughing; runs upstairs; automatic; fight† | | | |
| | | | | | G. Sexual | | | | | |
| 31 LNP | Noise enters body | → | Danger feeling | → | Patting on right; disrobing; sexual intercourse | → | G.S. | | | |
| 32 RFT | Visual delusion of animation | → | Palpitation; unreality | → | Vomit or orgasm | | | | | |
| 26 RAT | Perfume smell | → | Unreality; numb body, head | → | Fumbles with girls or self | → | G.S. | | | |
| | | | | | H. Olfactory—Pleasant | | | | | |
| 26 RAT | Perfume smell | → | Unreality; delusions | → | Numb body, head | → | Mumbles; passes at girls; fumbles with self or girls | → | G.S. | |
| 4 BiT | Sweet smell | → | Warm; flushed | → | Jumbled; confused | → | Smacking; chewing; strokes face; pallor, pupils dilated | → | | |
| 19 LTy | Sweet craving | → | Dizzy; tense | → | Mind griped | → | Chewing; smacking; eating automatism | → | G.S. | |
| | | | | | I. Illusion of Noise Entering Body | | | | | |
| 31 LNP | Noise enters body | → | Danger feeling | → | Patting objects on right; disrobes; sexual intercourse | → | G.S. | | | |
| 33 RAT | Noise enters body; visual hallucinations | → | Epigastric sensation | → | Walks rapidly disrobes; micturition | | | | | |

TABLE I.—*Summary of Content and Sequence of Individual Patient Attacks**
Continued

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | J. Procursive Epilepsy (Running Fits) | | | | | | | |
| 6<br>RNP | Gastric | → | Fear; indecision | → | Ears ring; hot & cold | → | Wants to grab; wants to run | → | Pallor; running; grabbing; snorting | | | |
| 3<br>RNP | Gastric | → | Fear | → | Odor, bad | → | "Must go" | → | Running; searching; fight† | → | G.S. | |
| 2<br>RT | Nausea | → | Fear | → | Bad odor; visions | → | | → | Running; fight† | → | G.S. | |
| 12<br>RT | Tinnitus; dizziness | → | Sound distorted | → | Fear | → | Bad odor; tongue tingles | → | "Dizzy head" | → | Running; fight† | → | G.S. |
| 33<br>RAT | Noise enters body; visions | → | Epigastric sensation | → | | → | | → | Walks rapidly; disrobes | | | | |
| 27<br>RPTP | Electricity, whole body | → | Anger | → | Visions of animals chasing | → | Must grab; must run | → | Runs; shouts for help; attacks | | | | |
| 24<br>RAT | Familiarity; strangeness | → | Insecure; foreboding; morbid; depressed | → | Disaster; can't go on | → | | → | Grabs; runs; shouts; attacks | → | G.S. | | |
| 25<br>LT | Racing thoughts | → | Out of world | → | Wants to be alone | → | Terror | → | Stamps; spits; runs, makes fists | | | | |

* In order that the various seizure patterns may be more readily appreciated, the attacks are grouped in separate tabulations according to the characteristics common to the group. Patients may appear in more than one subgroup because of a variety of symptoms or signs linking them with more than one seizure type. The abbreviation immediately beneath patient's initials refers to the scalp or basal site at which spiking or sharp activity was elicited on the electroencephalogram. ¶R, right; L, left; NP, nasopharyngeal; F, frontal; P, parietal; T, temporal; O, occipital; AT, anterior temporal; Ty, tympanic; Bi, bilateral; o, no focus demonstrated; G.S., generalized (grand mal) seizure.
† When restrained.

depersonalization, and revelation, as well as the reliving of past experience or memory.

The ictal motor patterns which may follow such experiences, or which may commence unheralded by any subjective warning, fall into the general categories of flight, fight, feeding, searching, and sexuality. Postictal automatic behavior is even more varied and is not often consistent from one seizure to the next. It is not always obvious when ictal automatism becomes postictal automatic behavior even when a continuous EEG recording is made.[1,8]

On the basis of these preliminary data, certain patterns of functional organization may be suggested. Although a common onset is apparent in numerous seizure patterns, the subsequent progress of the attack suggests diverging pathways of propagation, much like the spreading folds of a Japanese fan as one traces the creases from the handle. Thus the early stages of various attacks may be strikingly alike (as the gastric-fear sequence), but with spread of the electrical excitation more and more variability is often present.

The gastric aura is of particular interest because this appears to be the commonest warning symptom in the epilepsies. This sensation usually is described as a peculiar sense of pressure beneath the epigastrium which rises to the throat. Cortical electroencephalography typically demonstrates a discharging focus in the insula or deep in the temporal lobe in such persons.[9,10] The near-ubiquitous succession of the epigastric or gastric sensation by that of fear is particularly striking and suggests the indispensability of the somatic visceral sensation for the emotional experience. Immediately following the fear sensation, disagreeable olfactory sensation is commonest, although a variety of alternative experiences are also reported, particularly somatic sensation. When this group of symptoms (gastric-fear complex) is followed by delusional and hallucinatory states, these are universally unpleasant, indeed often dreadful in the extreme, causing panic and great distress. Motor activity following such seizures, when not immediately grand mal, suggests a painful emotional cataclysm and is represented by running, grabbing, snorting, and choking, and often fighting when restrained.

In contrast to this group, the three patients grouped under the initial symptom of cephalic aura all express feelings of anticipation, expectancy, or revelation, followed by smacking and chewing or jumbled speech. Indeed, two patients who experienced both aurae in different attacks (Patients 1 and 11) clearly separate their attacks into "head" and "stomach" types, and, in the words of one of the patients, "If it's bad, it knocks you in the stomach and you don't know what to do with it—if it's good, it usually goes right up to your head." Evidence of terror or excitement is not reported during or following these "cephalic" attacks.

Seizures commencing with initial bodily sensation are followed by intense feeling states of various types—"pressure, anger, far away"—accompanied by severe mental obfuscation and tension and followed by what we may call the "flight and fight" pattern. Two of the four patients in this group spontaneously attack others during attacks.

Olfactory seizures are clearly divisible into two groups, depending on whether the olfactory experience is pleasant or disagreeable. The unpleasant aura is never in this series a first symptom of attack, but always follows a train of one or two previous sensations, most commonly fear or anxiety, suggesting that the abnormal discharge does not initiate in the olfactory region but is commonly propagated there from a hypothetical "fear" center. This recalls the important studies of MacLean, Horwitz, and Robinson, who obtained in rabbit and monkey olfactory cortex responses to noxious stimuli which were indistinguishable from primary olfactory evoked potentials.[11] Succeeding the unpleasant olfactory experience, universally disagreeable subjective states are experienced, including depression, sorrow, and anxiety. Again the fight-flight responses commonly follow, and masticatory or feeding patterns are also common sequelae.

Pleasant olfactory experience, on the other hand, is an initial symptom in the attacks in which it occurs, and is followed by illusions and delusions and mental confusion and unreality. This is succeeded by automatism free of fight-flight components.

The aura of vertigo and tinnitus is remarkable because of the occurrence thereafter of a high incidence of illusional states, including three instances of feeling "sorry for someone." Again, the fear-fight-flight pattern is absent save in a single patient, whose seizures appear to "short circuit" from tinnitus and sound distortion to fear, followed, as is so characteristic, by unpleasant odor and the flight-fight pattern.

The occurrence of sexual behavior or experience in these spells is thus far sufficiently rare as to be difficult of analysis. Similar behavior has rarely been reported in connection with any evidence of focal abnormality in the human brain.* The warnings of the three patients describing such behavior are remarkable because of the presence of delusory or illusory state prior to the automatic sexual experience. Curious, again, is the similarity of aura in the two patients who repeatedly disrobe during automatism. Both these persons (Table 1J) describe a sensation of "noise entering the body" as the initial warning of the seizure. Such patients perceive external noise (actually present) to be suddenly specifically directed at them personally, not only into the ears but penetrating the entire body. This is followed by a feeling of danger (Patient 31) or its visceral counterpart in the epigastrium (Patient 33) prior to loss of consciousness and the disrobing automatism.† One of these patients (No. 33), when struck by a seizure in a public place, partially disrobed his child instead of himself, saving considerable embarrassment. There was total amnesia for the event, as is the rule for psychomotor automatism.

Procursive seizures are commonest following fear sensation and are considered here as part of the flight reaction (Table 1J). Such "running fits" in man have been allied to an acute stress response by Sisler et al.[15]

The relationship of the electroencephalographic abnormality to the varying seizure patterns is not a striking one in this group, doubtless in part due to the fact that we are recording at a distance from the cerebral discharging focus or foci from electrodes located on the lateral and basal skull.‡ In general, it can be said that the gastric aura is more commonly associated with basal spiking (5 of 13 cases) than is illusion (none of 6 cases) or tinnitus-vertigo (none of 7 cases).

## Comment

Several inferences may be advanced on the basis of these preliminary studies. There is a striking alternation of somatic and psychic states throughout the development of many seizures of the temporal region. This indicates not only strong interdependence of somatovisceral sensation and emotional state but the possible indispensability of the somatic experience for the appreciation of emotion, as suggested by James and Lange long ago.[17]

The vast majority of temporal lobe seizure patterns encompass sensations of fear, danger, and discomfort, as opposed to pleasure and expectancy, suggesting that more of the substance of the brain in this region is assigned to experiences relatively unpleasant or preparatory to primitive defense.

The repeated occurrence of fight, flight, fear, feeding, and searching behavior and the occasional incidence of sexual experiences during seizures arising from this region are of profound interest in relation to the function of the temporal lobes and the nose in macrosmatic animals. In such species the olfactory brain and its sensory

*Gastaut[12] and Schreiner and Kling[13] have reported hypersexuality in cats with limited lesions in the hippocampal-amygdalar regions.

†Disrobing has been described as part of the flight reaction in frenzy states of peculiarly afflicted persons in certain "primitive" cultures.[14]

‡The nasopharyngeal leads introduced by MacLean[16] were used in the study of each patient.

TABLE 2.—*Summary of Relationships of Ictal Visceral and Somatic Sensations to Psychic and Motor Seizure Manifestations**

| | | Fear | Flight | Fight | Search | Eat | Sex | Illus. | Halluc. | Delus. | Sorrow | Pleasure |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gastric | 13 | 10 | 5 | 4† | 3 | 1 | 0 | 3 | 4 | 1 | 0 | 0 |
| % | | 77 | 38 | 31 | 23 | 8 | 0 | 23 | 31 | 8 | 0 | 0 |
| Tinnitus-vertigo | 7 | 1 | 1 | 1 | 0 | 2 | 0 | 5 | 3 | 2 | 3 | 0 |
| % | | 14 | 14 | 14 | 0 | 29 | 0 | 72 | 43 | 29 | 43 | 0 |
| Body | 4 | 1 | 1 | 1 | 0 | 0 | 0 | | 2 | 4 | 0 | 0 |
| % | | 25 | 25 | 25 | 0 | 0 | 0 | | 50 | 100 | 0 | 0 |
| Cephalic | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 2 | 0 | 0 | 3 |
| % | | 0 | 0 | 0 | 33 | 0 | 0 | 67 | 67 | 0 | 0 | 100 |
| Bad odor | 8 | 5 | 3 | 3† | 1 | 3 | 0 | 4 | 1 | 0 | 1 | 0 |
| % | | 63 | 39 | 39 | 13 | 39 | 0 | 50 | 13 | 0 | 12 | 0 |
| Pleasant odor | 3 | 0 | 0 | 0 | 0 | 2 | 1 | 3‡ | 0 | 0 | 0 | 0 |
| % | | 0 | 0 | 0 | 0 | 67 | 33 | 100 | 0 | 0 | 0 | 0 |

* Note the correlation of gastric with fear sensation; tinnitus-vertigo with illusory states; bodily sensation with delusory experience; cephalic sensation with illusion and hallucination, and pleasurable states; unpleasant odor with fear, and pleasant odor with feeling and illusory experiences.
† When restrained.
‡ Sense of intense mental confusion.

inflow, the sense of smell, are strongly tied to the ritual and performance of these six vital survival patterns.

It may be hoped that further study of the sequence of psychosensory and psychomotor seizures may prove a clue not only to the functional anatomy of the temporal region but to the anatomy of emotion as well, as suggested by Papez [18] and MacLean.[19]

## Summary

The convulsive attacks of 40 patients with psychosensory or psychomotor epilepsy have been subjected to sequential content analysis. Certain patterns of seizure organization appear from such analysis, suggesting an ordered "march" of seizure manifestations in convulsive attacks originating in the temporal lobes and environs.

The varied subjective manifestations of individual attacks indicate strong relationship of epigastric sensation, subjective fear, and motor behavior of the flight-fight pattern. On the contrary, the small group of patients with cephalic aura experience relatively pleasant anticipatory states, free of fear components. Vertigo and tinnitus are followed by illusory states in three-fourths of the patients studied, and fear was present in only one of the seven patients in this group. The disagreeable odor characteristic of the "uncinate fit" never appeared as a first symptom of attack in the eight patients reporting this sensation, and most commonly succeeded the subjective state of fear. Olfactory aura of pleasant nature, much rarer, was always a first symptom of an attack, and was not followed by fear-flight-fight manifestations but always was succeeded by a sense of intense mental confusion.

Preliminary analysis of the content and sequence of this group of psychosensory and psychomotor attacks appears to offer a doorway into greater understanding of the organization of emotional feeling and expression.

University of Oregon Medical School.

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# Asynchronism of Electrical Activity of Frontal Lobes During Sleep

*A Late Sequel of Frontal Lobotomy*

C. L. ADAMS, E. L. GIBBS, and F. A. GIBBS, M.D., Chicago

Patients subjected to frontal lobotomy may show after operation focal slow activity and seizure discharges. Such changes are to be expected from local cortical trauma and as an irritative reaction to injury. However, they are neither inevitable nor characteristic results of frontal lobotomy. In many cases, as will be shown in this report, the waking electroencephalogram remains normal. Lennox and Coolidge [1] have reported an absence of frontal sleep spindles as a sequel of frontal lobotomy. In our experience the change, if any, consists of a reduction of frontal sleep spindles; in most cases this reduction is so slight as hardly to be evident even after close comparisons of pre- and postoperative recordings.

We have observed an electroencephalographic alteration after frontal lobotomy which is constant and characteristic, but it takes many months to develop. We are now reporting this for the first time in print * because we have only recently collected a sufficient number of cases that had been followed for the necessary length of time. This unique and characteristic abnormality consists of bilateral asynchronism of slow activity in the frontal areas during deep sleep. It does not appear until approximately 18 months after operation. Other sleep patterns are not disturbed; the biparietal humps and spindles of light sleep are usually present and retain their normal degree of bilateral synchronicity, and the slow activity of deep sleep has its normal appearance in all areas except the frontal areas.

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From the Logansport State Hospital, Logansport, Ind., and the Department of Neurology and Neurological Surgery, University of Illinois College of Medicine.

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## Material and Method

Electroencephalographic studies were carried out on 202 patients who had been subjected to bilateral frontal lobotomy. These were patients with severe psychosis who had been institutionalized for prolonged periods and who had not responded to any types of available therapy. In 1 case the operation was a prefrontal lobotomy; in 9 cases the "standard" frontal lobotomy was performed (through burr holes in the coronal region), and in 192 cases the operation was of the closed transorbital type. The time of recording with respect to the operation and the number of cases studied at each time are shown in Figure 1.

Recordings were made with solder disc electrodes fastened to the left and right frontal, parietal, occipital, and temporal areas. Recordings were monopolar; usually both ears were interconnected to form a common reference, but in some cases the reference electrode was placed on the chin, in the low occipital area, or on the chest. Electroencephalograms were interpreted according to the normative standards set forth in the "Atlas of Electroencephalography." [2]

## Results

Slow activity in the postoperative period was not a prominent finding, nor were seizure discharges common. If a reduction in 12-per-second frontal spindles occurred, it was not enough to be considered abnormal and was remarkable only if compared with the preoperative recording.

The pre- and postoperative recordings were astonishingly normal. No slow-wave

foci, diffuse slowing, or seizure activity was observed (Fig. 1).

At about the 18th month after surgery some patients began to show asynchrony of slow activity during sleep in the frontal areas (Figs. 1 and 2). This became more evident and was a more constant finding with increasing time after the 18th month. At 36 months all patients with frontal lobotomies had asynchrony of slow activity in the frontal areas during deep sleep (Figs. 1 and 4).

Figure 2 shows normal synchronous slow activity during deep sleep in both frontal areas 12 months postoperatively. At 18 months this frontal slow activity is asynchronous, and at 24 months the asynchronism is

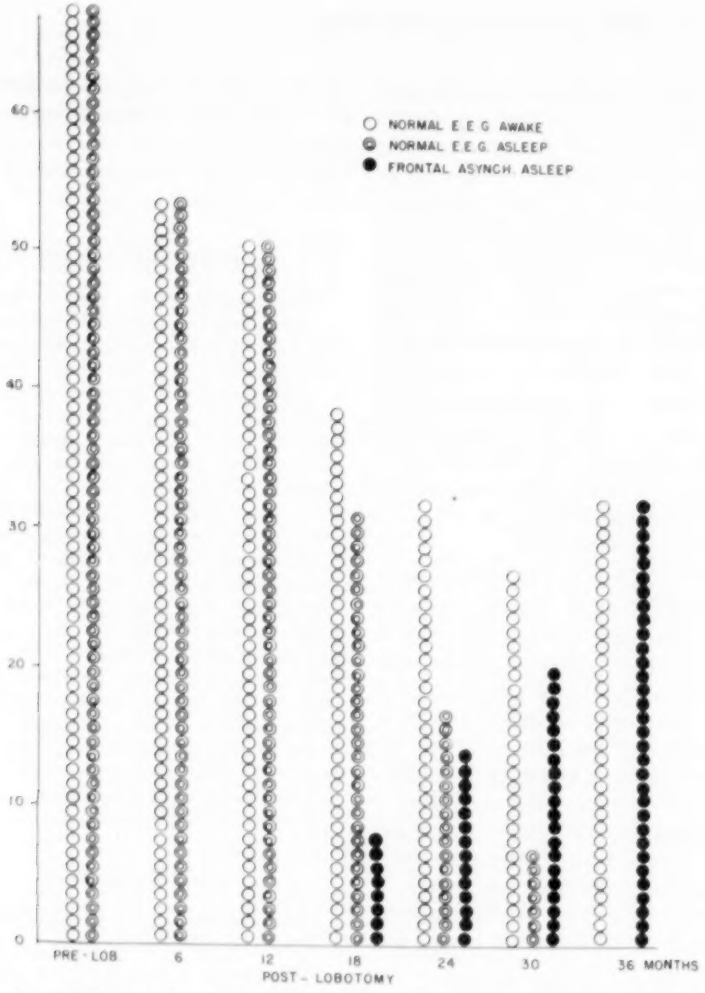


Fig. 1.—Relationship between the time after lobotomy and the incidence of frontal asynchrony during sleep. The abnormality does not appear until 18 months after lobotomy; from then on it becomes increasingly common, until at 36 months all patients on whom recordings were obtained showed abnormal frontal asynchrony, even though waking activity was entirely normal.

Each circle represents the electroencephalographic findings on one case at the time indicated. The decline in the total number of cases is not significant; it merely reflects the greater difficulty of obtaining follow-up recordings as the interval after lobotomy increases.

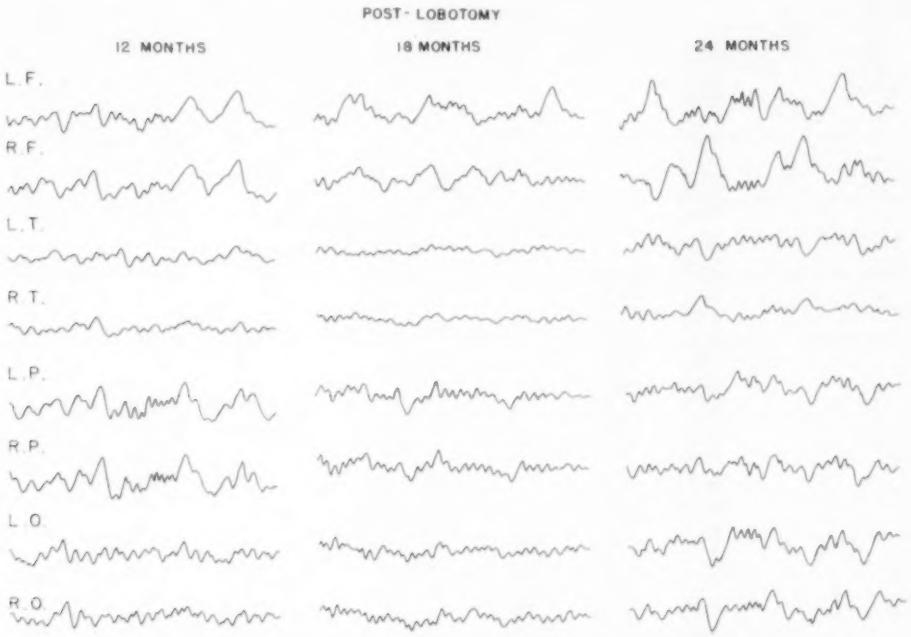


Fig. 2.—Normal synchronous slow activity in the frontal areas 12 months after lobotomy; abnormal frontal asynchrony 18 months after lobotomy; more evident asynchrony 24 months after lobotomy.

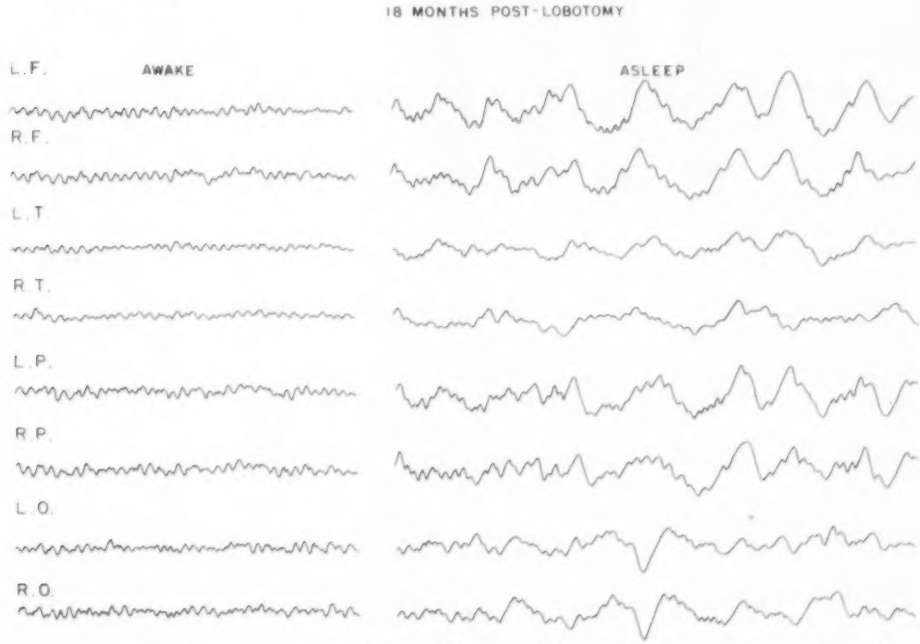


Fig. 3.—Eighteen months postlobotomy. Normal waking activity and synchronous frontal slow activity during deep sleep.

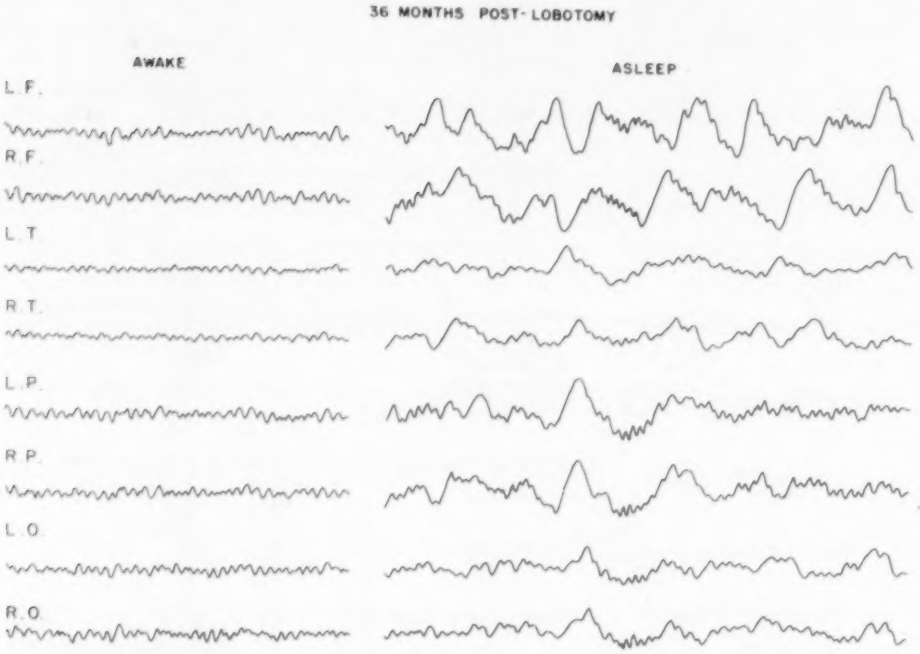


Fig. 4.—Thirty-six months postlobotomy (same patient as in Figure 3). Normal waking activity but marked asynchrony of frontal slow activity during sleep.

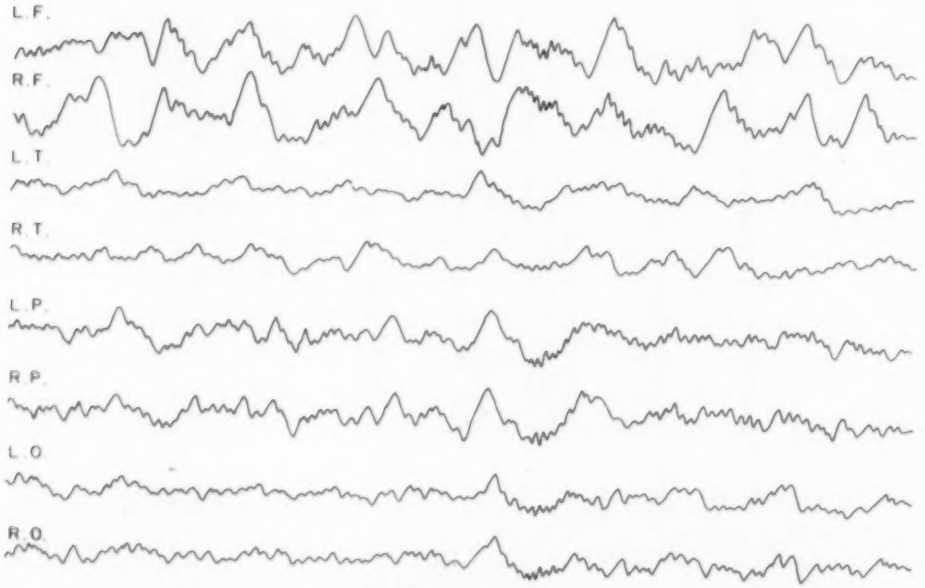


Fig. 5.—Thirty-six months postlobotomy (same patient as in Figure 3). Extreme asynchrony of frontal slow activity during sleep.

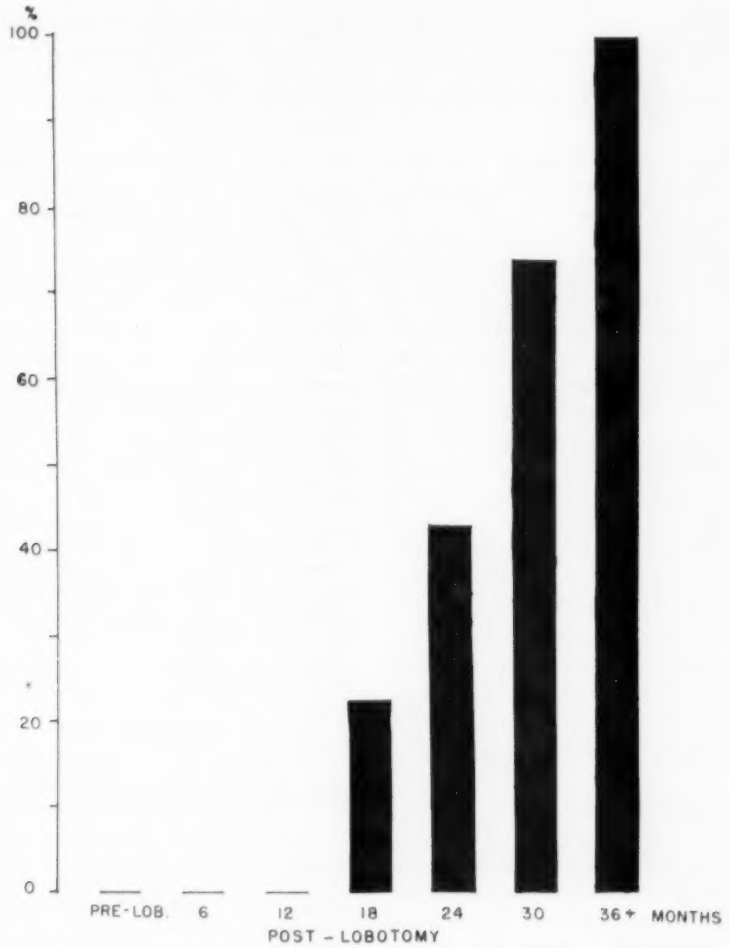


Fig. 6.—Percentage of patients with frontal asynchrony before and after lobotomy.

more evident. Figure 3 shows a case 18 months after lobotomy, with the usual normal waking electroencephalogram and with normal synchrony of slow activity still present in the frontal areas during deep sleep. Figure 4 shows that in this case a high degree of asynchronism of slow activity in deep sleep has developed in the frontal areas by the 36th month after lobotomy. Figure 5 is a 10-second sample of recording, showing independent slow activity in both frontal areas in a postlobotomy case 36 months after surgery. Fourteen-per-second spindles in the parietal areas and 12-per-second spindles in the frontal areas retain the normal degree of synchronicity. Slow activity in all other areas, except the frontal, retains a normal degree of synchronicity during deep sleep.

As far as we can ascertain, the only constant and reliable electroencephalographic evidence that a frontal lobotomy has been performed is the development of frontal asnychronism during deep sleep. This never appears before the 18th month and is invariably present 36 months after operation. The percentage incidence of frontal asynchrony

in sleep before and at various times after lobotomy is shown in Figure 6.

## Comment

The weight of the available evidence suggests that sleep patterns are developed in the thalamus and projected to the cortex.[3] The most likely hypothesis for explaining the independence of frontal slow activity as a late result of frontal lobotomy would seem to be the following: Delayed degeneration of commissural fibers which tie together the activity of certain thalamic nuclei in the left and right thalamus results in a functional separation. As a consequence, the slow activity which these nuclei generate in deep sleep is projected independently to the left and the right frontal pole.

The degeneration is apparently specific for certain nuclei and certain commissural fibers, because the synchronism of other patterns in the frontal lobes remains unaltered and the activity of other brain areas retains a normal degree of synchrony.

## Summary and Conclusions

Electroencephalographic studies on 202 patients with frontal lobotomy indicate that the only consistent electroencephalographic finding resulting from this operation is an asynchronism of slow activity in the frontal areas during deep sleep. This abnormality never appears before the 18th postoperative month. It becomes increasingly common and evident thereafter and is found in all cases 36 months or more after operation. This change is permanent and irreversible. The abnormality is restricted to the frontal lobes, and only the slow activity of deep sleep in the frontal lobes is affected. Sleep spindles and all other patterns in the frontal areas and elsewhere remain normal; in other areas the slow activity of deep sleep is undisturbed.

It is assumed that this late-appearing asynchronism of slow activity in the frontal areas during deep sleep results from a delayed degeneration of commissural fibers which link certain nuclei in the left and right thalamus.

Dr. John A. Larson, formerly superintendent of the Logansport State Hospital, organized and promoted this collaborative effort. Without his help it would not have been undertaken, and without his continuing support it could not have been completed.

Department of Neurology, University of Illinois College of Medicine.

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# Chlorpromazine (Thorazine) Treatment of Disturbed Epileptic Patients

VINCENT I. BONAFEDE, M.D., Sonyea, N. Y.

One hundred sixty-five disturbed epileptics of ages from 3 to 69 years have been treated at Craig Colony with chlorpromazine for periods varying from 2 to 12 months, the majority of whom are female. This series includes a group of 78 patients on whom a preliminary report [1] was submitted about a year ago and a supplemental group of 87 patients. The length of treatment is shown in Table 1.

Selection for therapy was based on behavior and emotional disturbances, episodic and chronic, clinically manifested by irritability, excitement states, temper outbursts, furor states, restlessness, overactivity, resistiveness, destructiveness, assaultiveness, nakedness, aggression (such as biting, scratching, and pulling hair of self and others), self-mutilation, noisiness, profanity, night wandering, filthy habits, and active psychotic trends. Many frequently required large doses of sedation or some form of restraint or seclusion. The overwhelming majority of patients are mentally defective, with 21 idiots, 47 imbeciles, 46 morons, 47 borderline normals, and 4 normals. The epileptic disorder had been present in 53% from 20 to 49 years, in 4% from 50 to 66 years, in 28% from 10 to 19 years, and in 15% from 2 to 9 years. Hospitalization has also been lengthy, with 26% in residence less than 4 years, 18% from 5 to 9 years, 33% from 10 to 19 years, 19% from 20 to 29 years, and 4% from 30 to 45 years.

The epilepsies were classified as shown in Table 2.

TABLE 1.—*Length of Treatment*

| Treatment Period, Mo. | No. | Treatment Period, Mo. | No. |
|---|---|---|---|
| 2 | 6 | 8 | 1 |
| 3 | 26 | 9 | 3 |
| 4 | 33 | 10 | 2 |
| 5 | 14 | 11 | 16 |
| 6 | 6 | 12 | 48 |
| 7 | 10 | ... | ... |

TABLE 2.—*Classification of Epilepsies*

| | No. of Patients |
|---|---|
| Idiopathic | 116 |
| Symptomatic | 49 |
| Agenesis and birth injuries | 15 |
| Meningoencephalitis | 20 |
| Postnatal trauma | 7 |
| Metabolic defects | 2 |
| Congenital syphilis | 2 |
| Tuberous sclerosis | 2 |
| Endocrinopathy | 1 |

## Technique of Administration

Chlorpromazine was administered daily in various doses ranging from 50 to 300 mg., except in the cases of acute excitement, in which, because of their resistance to oral medication, an initial parenteral dose of 100-150 mg. was given. Small doses were, in general, unsatisfactory, and our best therapeutic results were obtained when therapy was begun with a dose of 200-300 mg., with the dose increased or decreased, in proportion to the clinical response, at weekly or biweekly intervals. On the basis of our experience in this series, it is our opinion that treatment should be discontinued if no satisfactory response is gained after a trial of four months, as improvement thereafter is doubtful. The maintenance dose was extremely variable. Very few patients were able to maintain their improvement on daily doses of less than 100 mg. In general, most were maintained on a daily dose of 200-400 mg., with a few requiring as high as 600 mg. daily.

All of these patients received phenobarbital alone or in combination with other anticonvulsants,

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133 receiving a dose of 3 to 6 grains (180 to 360 mg.) of phenobarbital daily. We have learned through this study that at any indication of a seizure increase it is essential and vital that anticonvulsant medication be increased immediately and supplemented with other anticonvulsants; otherwise the homeostatic balance may be so disrupted as to make effective control difficult to reestablish. If any doubt exists, chlorpromazine should be discontinued promptly.

## Results

Four problems occupied our principal interest in this study: 1. Was chlorpromazine of any value in controlling episodic and chronically disturbed epileptics? 2. What effect would chlorpromazine have on altering the previous seizure frequency? 3. Would there be any potentiation of barbiturates and to what degree? 4. What complications would develop?

Our original group of 78 patients on whom we previously made a report has now been treated with chlorpromazine for a period of 11-12 months, with the exception of 14 who were dropped earlier, for the following reasons: coma, 1; death, 1; recurrent fever and rash, 1; release on convalescent status, 14, and poor clinical response, 7. This series of 78 patients was initially subdivided into three groups, but in two of these groups the dose of phenobarbital was reduced one-third and one-half, respectively, because of the possibility of its potentiation by chlorpromazine. We were well aware that the reduction of phenobarbital might well lead to the hazard of an increase in seizures or status epilepticus, but the behavior and conduct disorders of these patients were such a serious problem in management that treatment with any drug that offered a modicum of hope was worth a therapeutic trial. Any risk, however, was minimized by keeping the patients under close supervision on closed wards. In half of the patients in whom phenobarbital had been reduced, we had to return to the original dose of phenobarbital and also, in some, add other anticonvulsants, in an attempt to maintain the previous therapeutic level.

Evaluation of behavior was determined by personal knowledge and consultation with the ward physician, ward supervisors, nurses, and attendants, who were in daily contact with the patients. The behavior response was essentially the same as previously reported [1] in the moderately and markedly improved groups, although there was some shifting in the degree of response in some of the patients in all groups. In the unimproved group, doses as high as 1000-1500 mg. daily were used. Table 3 reveals the statistical data on the behavior response of the 64 patients who were carried and maintained on chlorpromazine for 11-12 months. The results unquestionably demonstrate the therapeutic efficacy of chlorpromazine in controlling behavior and conduct disorders of chronically disturbed epileptics.

Evaluation of seizures was based on a comparison of their number and frequency in the period under treatment with their previous five-year record, and the results are tabulated in Table 4.

The 10 patients listed in Table 4 as showing no seizures were persons whose seizures had been well controlled for a varying number of years and served as an excellent control in determining whether or not chlorpromazine had any epileptogenic property. Our results reveal that all of the 64 patients under treatment for 11-12 months except 19 showed the occurrence of no convulsions, no change in their previous frequency, or a reduction of seizures as compared with their previous five-year record. The increase in

TABLE 3.—*Behavior Responses*

| Behavior Responses | Phenobarbital Reduction | | | Total | % |
|---|---|---|---|---|---|
| | None | 33.3% | 50% | | |
| Markedly improved | 6 | 8 | 15 | 29 | 45.3 |
| Moderately improved | 6 | 10 | 3 | 19 | 29.7 |
| Slightly improved | 4 | 2 | .. | 6 | 9.4 |
| Unimproved | 5 | 2 | 3 | 10 | 15.6 |

TABLE 4.—*Results in Sixty-Four Patients Under Treatment for Ten to Twelve Months*

| Seizure Response | Phenobarbital Reduction | | | Total |
|---|---|---|---|---|
| | None | 33.3% | 50% | |
| No seizures | 5 | 2 | 3 | 10 |
| No change in frequency | 6 | 5 | 8 | 19 |
| Slight increase | ... | 3 | 2 | 5 |
| Moderate increase | 1 | 3 | 3 | 7 |
| Marked increase | ... | 3 | 4 | 7 |
| Slight reduction | 1 | ... | 1 | 2 |
| Moderate reduction | 5 | 3 | ... | 8 |
| Marked reduction | 3 | 3 | ... | 6 |

seizures, when it did occur, was significant and prominent in the groups in which we had originally reduced the phenobarbital, and consequently we feel it is reasonable and logical to conclude that the seizure increase was due primarily to the reduction of phenobarbital rather than to any action of chlorpromazine. Nevertheless, we wish to emphasize that whenever there is any sign of an increase in seizures in epileptics under chlorpromazine therapy, it is imperative to increase their current anticonvulsant medication or supplement it with another anticonvulsant and, if any doubt exists, chlorpromazine should be dropped. In 7 of 19 patients showing an aggravation in the number of seizures, the increase was manifest within the first 14 days, the increase in most instances beginning the day phenobarbital was reduced and chlorpromazine started. Two patients showed an increase in their seizures within 20-30 days and one in approximately 40 days. In the others the increases occurred as late as four to six months after treatment was started or were spread out. A return to the prechlorpromazine seizure frequency was reestablished in 8 out of the 19 patients, but in the remaining 11 patients the seizure increase was a problem only in 6, in whom a diminution in the frequency was difficult to obtain, despite supplementary anticonvulsant medication.

TABLE 5.—*Seizure Response in Eighty-Seven Cases*

| | |
|---|---|
| No seizures | 23 |
| No change in frequency | 55 |
| Slight increase | 2 |
| Moderate increase | 2 |
| Marked increase | 1 |
| Slight reduction | 1 |
| Moderate reduction | 1 |
| Marked reduction | 2 |

One can only speculate on why 16 patients showed an appreciable reduction in the number of seizures. Coincidence may have been a factor in a few, but in the others it seems plausible to assume that the reduction was associated with a diminution in tension and anxiety, inasmuch as chlorpromazine is not known to have any anticonvulsive property. It is also of interest to note that many patients reported the disappearance of aura while under treatment.

In the supplemental group phenobarbital was not reduced. The results (Table 5) show that 78 of the 87 patients treated for periods varying from 2 to 10 months had no seizures or any change in the frequency of seizures; consequently, it seems reasonable to conclude that when effective anticonvulsant control is maintained, any alteration in the seizure frequency of epileptics is minimal under chlorpromazine treatment. Behavior response (Table 6) was also excellent, over three-fourths showing some degree of improvement. In this series, 19 children, of both sexes, under the age of 15 years, were treated. Nine were less than 10 years old and ten between the ages 10 and 15 years. Doses of chlorpromazine as high as 400 mg. were given, and three children, aged 4 to 5 years, were maintained on 300 mg. daily, without any complications. All of the children save two showed a significant improvement.

TABLE 6.—*Behavior Response in Eighty-Seven Patients*

| | No. | % |
|---|---|---|
| Marked improvement | 21 | 24.14 |
| Moderate improvement | 28 | 32.18 |
| Slight improvement | 19 | 21.84 |
| Unimproved | 19 | 21.84 |

## Weight

The majority of the patients continued to show a progressive gain in weight (Table 7); consequently, this has lead to resistance among some of the female patients to the extent that newly admitted patients are forewarned and, if suitable for therapy, plead to avoid being placed on it.

TABLE 7.—*Weight Gains in 165 Patients*

| Gain, Lb. | No. of Patients |
|---|---|
| 0 | 15 |
| − 2 to − 9 | 15 |
| + 2 to + 9 | 57 |
| +10 to +19 | 40 |
| +20 to +29 | 20 |
| +30 to +39 | 9 |
| +40 to +49 | 6 |
| +50 to +59 | 2 |
| +65 | 1 |

## Complications

The only complications not previously reported in the initial group of 78 patients [1] were Parkinsonoid facies, 2; rash, 1, and minimal myoclonic convulsions, 3. In the supplementary group (87 patients) the following complications were observed: Parkinsonoid facies, 4; myoclonia, 2; jaundice, 1; facial edema, 2, and oral dermatitis, 1. The last was the result of contact with a chewed tablet, after which excoriations of the mucous membrane of the lips and palate developed, together with an erythematous macular eruption of the skin at the corners of the mouth and upper lip. A case of herpes zoster and stillbirth of a macerated fetus are two unusual occurrences noticed during treatment. There is, however, no conclusive evidence to indicate any casual relationship to chlorpromazine. The stillbirth occurred in a Secundigravida unipara, who received chlorpromazine totaling 31,000 mg. during the last seven months of her pregnancy. Fetal heartbeats had never been heard.

The absence of motor incoordination, ataxia, and marked drowsiness seemed to indicate that potentiation of barbiturate effect is apparently of little or no clinical significance.

## Summary and Conclusions

The majority of emotionally disturbed epileptics show an excellent response to chlorpromazine.

Anticonvulsant medication must never be reduced while the patient is on chlorpromazine therapy.

Potentiation or intensification of barbiturate effect is apparently of little or no clinical significance.

Anticonvulsant drugs should be increased or supplemented at the earliest indication of any seizure increase during chlorpromazine therapy.

Chlorpromazine is well tolerated, without any marked alteration in the seizure frequency in most epileptics.

Maintenance dosage is established by trial and error and may be necessary for prolonged periods.

Craig Colony.

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# The Pattern of Conduction of Amygdaloid Seizure Discharge

*An Experimental Study in the Cat*

P. GLOOR, M.D., Montreal, Canada

## Introduction

Among the clinical manifestations of focal epileptic discharge, one of the most interesting and least understood phenomena is certainly that of ictal epileptic automatism. Hughlings Jackson and Colman, in 1898,[1] were the first to recognize that this epileptic manifestation oftenest had its origin in the uncinate gyrus, though they considered the automatism to be postictal.

Jasper[2]; Gastaut and associates,[3,4] and Jasper, Pertuiset, and Flanigin[5] arrived at similar conclusions on the basis of electrographic studies and incriminated deep temporal structures, especially the rhinencephalic formations of the temporal lobe, as the possible locus of origin of the discharge resulting in so-called "psychomotor" attacks. Recent investigations by Feindel, Penfield, and Jasper[6] confirmed this opinion and suggested that ictal automatism most frequently depends upon focal discharge originating in the region of the amygdala.[7] It is also from this region that, in patients undergoing surgical treatment for epileptic attacks, the disturbances in consciousness and other phenomena characterizing epileptic automatism were frequently reproduced by electrical stimulation.

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The automatic state is characterized clinically by a varying degree of clouding of consciousness, together with "complete loss of capacity to make durable memory records" (Penfield and Jasper[8]). This goes along with preserved motor control and some degree of preservation of adequate reaction to the environment. This seems to indicate that epileptic discharge originating in the amygdaloid region finds an easy way to be propagated into structures regulating highly integrative processes of the nervous system, thus producing a profound disorganization of their complex functions. This led Penfield[9] to postulate a close relationship between the amygdaloid region and the central integrating structures of the higher brain stem, for which he coined the term "centrencephalic integrating system."

Routine EEG examinations of patients with temporal lobe automatism most frequently show a focal area of discharge in the anterior temporal region, extending into the mesiobasal aspect of the temporal, as seen with pharyngeal lead recordings.[3,5,7,10-14] This observation is confirmed by the findings obtained in electrocorticography from the exposed cortex. Human studies employing deep electrical stimulation and postexcision recordings after removal of the tip of the temporal lobe suggest that the main focus of abnormality is situated in the region of the amygdaloid complex (Feindel and Penfield[7]). The epileptogenic activity seen in routine EEG and in surface electrocorticography on the intact brain therefore seems to be a projected disturbance from a deeper-lying triggering focus in the amygdaloid area.

The present study was undertaken to elucidate some of the problems and hypotheses raised by these clinical and electroencephalographic observations. Local epileptic discharge was produced in the amygdala in cats by electrical stimulation, and the conduction of this locally evoked seizure activity into cortical and subcortical areas was systematically studied. In this study the local amygdaloid after-discharge produced by electrical stimulation will be considered as the equivalent of a local amygdaloid seizure discharge. It is assumed that its conduction to distant areas might equate the pattern of propagation of a spontaneous amygdaloid seizure discharge.

## Method

The experiments reported in this paper were carried out on 19 cats anesthetized with pentobarbital (Nembutal) given intraperitoneally. In most of the experiments the level of anesthesia was kept light in order to study the animal under conditions reasonably close to normal. In some experiments deep anesthesia was used in order to study its effect on the conduction of seizure activity.

Cortical records were taken with bipolar or monopolar technique using silver-ball electrodes resting gently on the surface of the pia. In monopolar recordings the indifferent electrode was attached to the occipital bone. The deep stimulating and recording electrodes were steel needles insulated except at the very tip. The electrode inserted into the amygdala was a two-needle electrode with a distance of 0.5-1 mm. between the tips. This electrode was inserted in a parasagittal plane in order to ensure, as much as possible, that the two tips were located in the same nuclear subdivision of the amygdala. The subcortical pick-up electrodes were four-needle electrodes with either 1 or 1.5 mm. interelectrode distances. They were inserted vertically in a frontal plane, or occasionally from the posterior fossa in a caudo-rostral direction. Most of the subcortical recordings were bipolar, but some were monopolar records using the same occipital reference electrode as for the cortical monopolar records.

In order to allow the accurate observation of local seizure activity, the amygdaloid after-discharge was recorded immediately after the end of stimulation through the same electrodes used for stimulation. This was made possible by a switch allowing the connecting of the amygdaloid electrodes at will either to the stimulator or to the recording unit. All records were taken on paper with a six-channel Offner dynograph.

Stimulation was delivered with a square-wave generator, allowing independent control of all parameters of stimulation. The stimulation artifact was reduced as much as possible by the use of a radio frequency isolation unit. Stimulation of the amygdala was carried out with pulses of 10-msec. duration at a frequency of 40 cps. The intensity of stimulation was adapted to the state of excitability of the animal. First, the threshold intensity at which a local amygdaloid after-discharge could be produced was established. At the very threshold the local after-discharge was usually very short, consisting most of the time of one or two single discharges occurring after the end of the stimulation volley (Figs. 1 and 4). It was usually necessary to raise the stimulation voltage to a level about 0.5 to 2 volts higher in order to obtain a fully developed, self-sustained after-discharge. As a rule these after-discharges, produced with slightly suprathreshold stimulation, were used to study the conduction of abnormal discharge to cortical and subcortical areas. The voltage range of this type of stimulation varied rather widely from one animal to the other between the extreme values of 1.5 and 20 volts, depending on the state of excitability of the preparation. The higher threshold values were found in animals having suffered considerable blood loss or in those submitted to deep anesthesia. Figure 1 shows how such threshold determinations were carried out. In this animal stimulation of the basolateral nuclear complex of the amygdala with 13 volts produced no after-discharge. Stimulation with 13.5 volts yielded a single amygdaloid discharge after cessation of stimulation, which may possibly have been reflected in the first channel recording from the medial geniculate body, as shown by the arrow. There was still no cortical effect, as seen in the records from the sensory-motor and Sylvian areas. The local after-discharge was not sustained. Stimulation with 14 volts, however, produced a well-sustained local amygdaloid after-discharge in the area stimulated, and this was conducted to the thalamus—in this instance the medial geniculate body—and to the Sylvian cortex, but the sensory-motor cortex was still not involved in the after-discharge.

In order to keep the after-discharges constant and to avoid, as much as possible, fluctuations in threshold due to neuronal fatigue, the duration of stimulation was invariably five seconds, and an interval of five minutes was always observed between each of the succeeding stimulations.

Stimulations were mostly carried out in the basolateral nuclear group; in some instances also in the anterior amygdaloid area and in the corti-

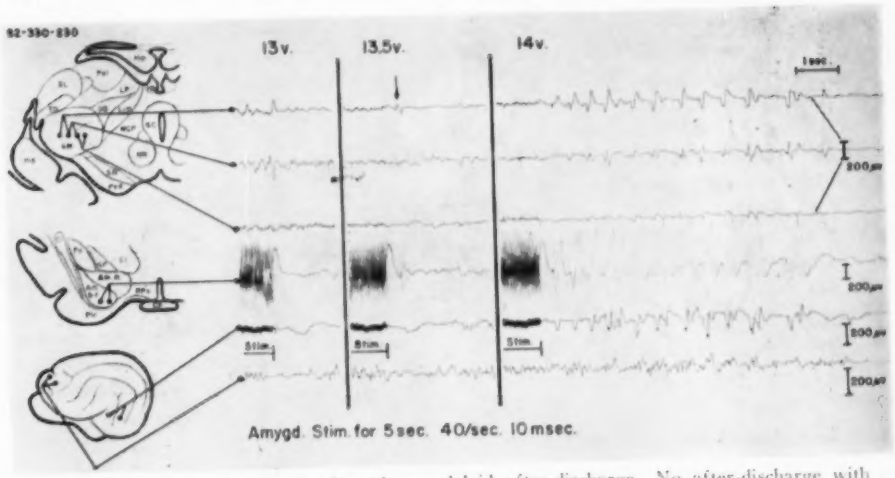



Fig. 1.—Threshold determination of amygdaloid after-discharge. No after-discharge with 13-volt stimulation; one single discharge with 13.5 volts, possibly reflected in the record from the medial geniculate body (arrow). Fully developed after-discharge with 14-volt stimulation. After-discharge is conducted to the ipsilateral thalamus (medial geniculate body) and to the "insular" cortex.

The following abbreviations appear in this Figure and in the accompanying Figures: *AM*, N. anteromedialis; *AM. b-l*, amygdala, basolateral nucleus; *AM. m.*, amygdala, corticomedial nucleus; *AV*, N. anteroventralis; *CC*, corpus callosum; *Cd*, caudate nucleus; *Ch*, chiasma opticum; *CI*, internal capsule; *Cl*, claustrum; *En*, entopeduncular nucleus; *Fx*, fornix; *Gc*, central gray matter; *Gl*, lateral geniculate body; *GM*, medial geniculate body; *GP*, globus pallidus; *H*, Forel's field H; *Hb*, habenular nucleus; *Hd*, dorsal hypothalamic nucleus; *Hip*, hippocampus; *Hl*, hypothalamus lateralis; *Hy*, hypothalamus; *IC*, inferior colliculus; *LD*, N. lateralis dorsalis; *Lim*, N. limitans; *LP*, N. lateralis posterior; *MD*, N. medialis dorsalis; *MFB*, medial forebrain bundle; *Mm*, mammillary body; *NCM*, N. commissurae posterioris; *NHvm*, N. ventromedialis hypothalami; *NR*, red nucleus; *P*, cerebral peduncle; *Pir*, piriform cortex; *Pu*, putamen; *Pul*, pulvinar; *Pc*, N. paracentralis; *Ped*, cerebral peduncle; *PVH*, paraventricular nucleus of hypothalamus; *P*, pyramidal tract; *R*, N. reticularis thalami; *Re*, N. reuniens; *Ret*, reticular formation; *Rh*, N. rhomboideus; *RPo*, preoptic region; *S*, stria medullaris thalami; *SG*, N. suprageniculatus; *SN*, substantia nigra; *St*, stria terminalis; *TO*, tractus opticus; *VA*, N. ventralis anterior; *VL*, N. ventralis lateralis; *VM*, N. ventralis medialis; *VPL*, N. ventralis posterolateralis; *VPM*, N. ventralis posteromedialis; *ZI*, zona incerta.

comedial group. Stimulations in these different areas of the amygdala did not give significantly different results.

Electrode positions in the brain were marked with a small D. C. current and then stained with the potassium ferrocyanate method. All brains were fixed in formalin and sectioned. The histological preparations were stained for cells and fibers. The electrode positions and the recorded responses were plotted according to the "Atlas" of Jasper and Ajmone-Marsan.[16]

## Results

The results obtained by this method of investigation indicate that seizure discharge originating in the amygdala of the cat is characterized by a very diffuse and extensive subcortical conduction, to which the restricted cortical firing appears in rather sharp contrast.

In most instances the local amygdaloid after-discharge was conducted to a surprisingly wide subcortical area on the ipsilateral side, comprising the septum, the hypothalamus, the subthalamus, the thalamus (Fig. 2), and the upper brain stem. Quite on the contrary to this, the cortical involvement was restricted to areas homologous to the cortex of the anterior and mesial parts of the temporal lobe and the insula of man. These were represented by the lower part of the posterior ectosylvian and the anterior and posterior Sylvian gyrus. These neocortical areas will be referred to hereafter as "temporoinsular" cortex.

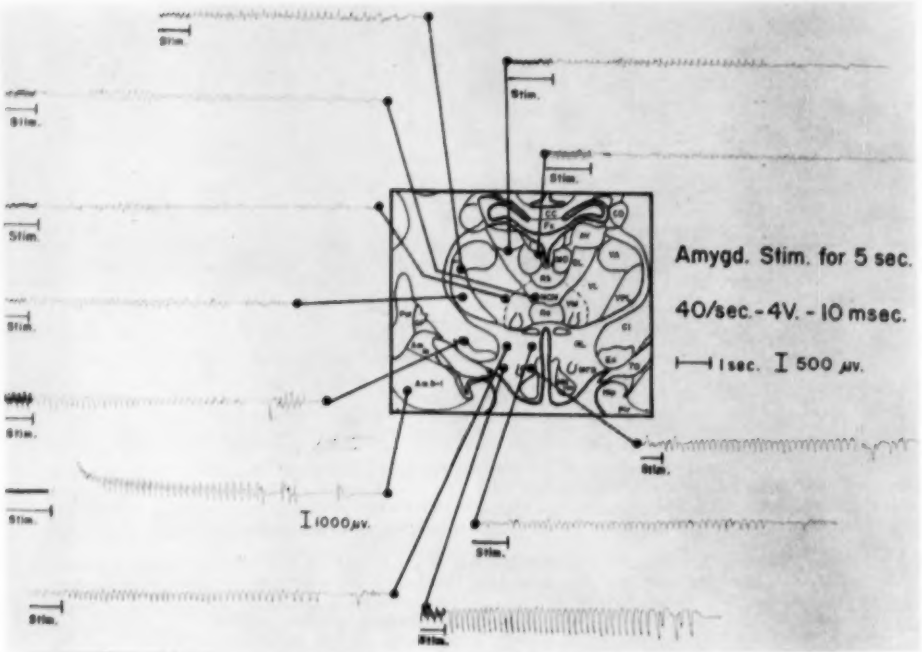



Fig. 2.—Diffuse diencephalic conduction of amygdaloid after-discharge. Higher-amplitude discharges are seen in the hypothalamus. The local after-discharge in the amygdala shows a spike-and-wave pattern at 5-6 cps. (The different samples are from different subsequent stimulations, all producing a constant after-discharge locally in the amygdala.)

The hippocampus also showed very high-amplitude after-discharges when a local amygdaloid after-discharge was induced.

Less constantly, but still quite often, after-discharges were recorded in the ipsilateral anterior limbic cortex. Only in a few cases were they recorded in the ipsilateral sensory-motor cortex. Their occurrence, though rare, was interesting insofar as it took place long before any other neocortical area outside the aforementioned "temporoinsular" and anterior limbic cortices was involved.

In view of the frequent occurrence of bilateral temporal lobe disturbances in patients with epileptogenic foci in the amygdaloid region, it was rather unexpected to find that in our experimental animals the opposite amygdala seemed to take part in the after-discharge only when higher stimulation voltages were applied. This suggests that seizure discharge may actually impinge upon widespread ipsilateral subcortical areas before there is any appreciable firing into deep temporal structures of the contralateral side.

Contralateral subcortical recording in brain stem and diencephalon was carried out in only two animals. One showed no contralateral involvement; the other, some very low-voltage after-discharges in the opposite thalamus, hypothalamus, subthalamus, and mesencephalic tegmentum.

The cortex of the opposite side, when fired at all, showed the same localization of the after-discharge as the homolateral side; i. e., the areas involved were the contralateral "temporoinsular" cortex. To produce conduction of the after-discharge to the contralateral cortical projection area, still higher intensities were required than for firing the contralateral amygdala.

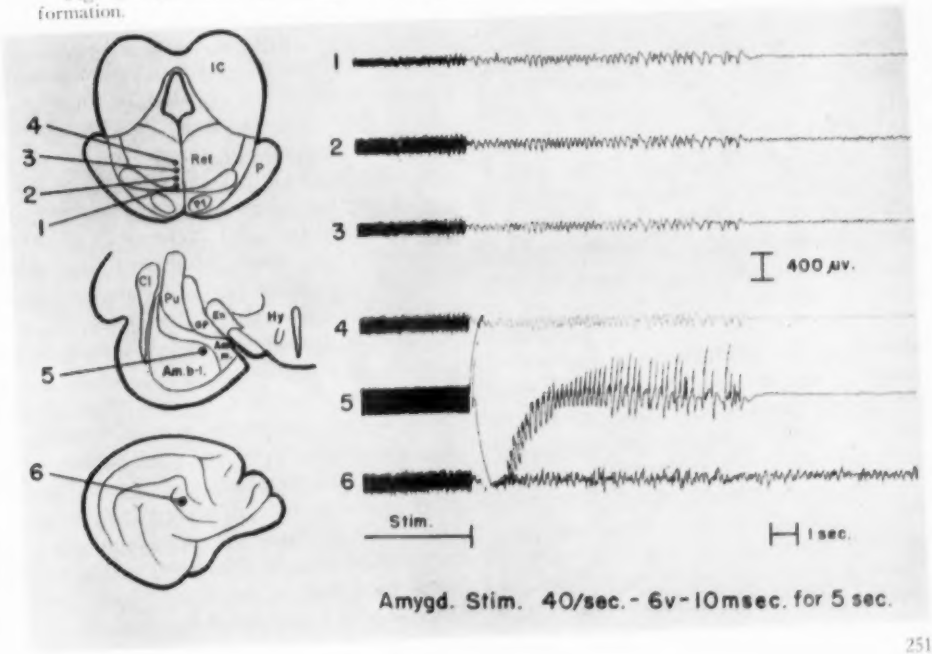
The widespread and diffuse involvement of subcortical structures in amygdaloid seizure activity was an unexpected and somewhat puzzling finding. Some doubts as to its reliability had to be dissipated before the fact could be accepted that a local after-

discharge in the amygdala was able to fire such an extensive subcortical area, reaching from the septal region to the mesencephalon and including the whole diencephalon. The restricted character of the cortical conduction of amygdaloid after-discharges, however, ruled out the possibility of a generalized electrographic seizure. Moreover, a control stimulation was carried out in the posterior suprasylvian gyrus in an animal showing a threshold of 4 volts for setting up an amygdaloid after-discharge. The thalamic recording electrodes were placed outside the thalamic projection area of the posterior suprasylvian gyrus. No after-discharge was picked up with the thalamic leads or in the motor cortex, despite the fact that stimulation intensity was raised up to 12 and 14 volts. Yet the record of the stimulated posterior suprasylvian cortex showed a fully developed after-discharge. This, again, suggests that the diffuse subcortical conduction of amygdaloid after-discharges is a genuine fact and not an unspecific effect of overstimulation.

The lowest level in the brain stem where after-discharge could be recorded varied with the state of excitability of the animal, depending on factors like depth of anesthesia, blood loss, and so forth. Clear after-discharges could normally be picked up as far as the lower part of the tegmentum mesencephali, as shown in Figure 3, where a well-developed after-discharge was recorded in the reticular formation of the lower mesencephalon. Toward the pontobulbar level, the after-discharges tended to fade away, and only occasionally could they still be recorded at a true bulbar level.

Although this diffuse involvement of diencephalic and mesencephalic structures was the rule, some rarer observations made under conditions of less intense seizure activity or of lowered cerebral excitability were of great importance in pointing out the preferential pathways of conduction of amygdaloid seizure discharge. Thus the possible mechanism of the diffuse subcortical propagation of amygdaloid seizure activity became more understandable.

Fig. 3.—Conduction of amygdaloid after-discharge into lower mesencephalic reticular formation.



Less intense seizure activity was sometimes the result of stimulation with threshold intensity. Local amygdaloid after-discharges produced by such threshold-intensity stimulations were sometimes very short and difficult to follow in their propagation to other areas. In some instances, however, they were conducted to subcortical structures and were then often more clearly seen in the hypothalamus, subthalamus, and brain stem reticular formation than in the thalamus. Conduction of these minimal epileptic disturbances to cortical areas was even much more inconstant. Figure 4 shows an example of this. A short local amygdaloid after-discharge which fired the subthalamus failed to fire the Sylvian cortex, although this cortical area was almost regularly involved when the local amygdaloid after-discharge was more sustained.

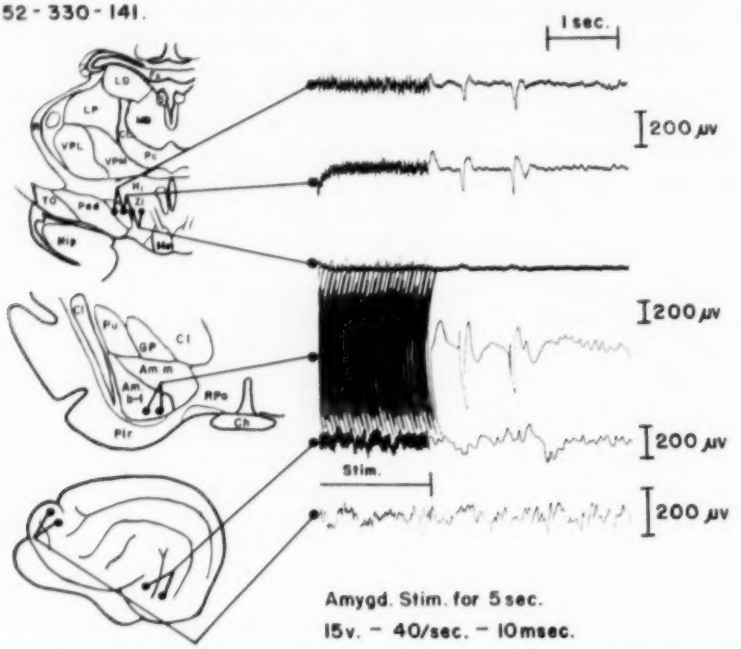



Fig. 4.—Short amygdaloid after-discharge conducted to subthalamus but not propagated to ipsilateral "insular" cortex.

Preferential propagation of amygdaloid epileptic disturbance to subcortical areas rather than to the cortex is also shown in Figure 5, which is from an experiment carried out under deep anesthesia. Under these conditions conduction to cortical areas was inhibited; no cortical after-discharge was seen, even in such areas as the inferior portion of the posterior ectosylvian gyrus and the posterior Sylvian gyrus, which almost constantly participated in an amygdaloid after-discharge under light anesthesia. Yet the hypothalamus showed a very clear after-discharge.

Similar conditions were encountered in other situations with depressed cerebral activity, e. g., when insufficient time was allowed for recovery of the brain after stimulation followed by after-discharge, or in animals having suffered a considerable amount of blood loss.

All these factors, i. e., low intensity of the initiating amygdaloid seizure discharge, deep anesthesia, blood loss, and fatigue, not only depressed the conduction of amygdaloid after-discharge to cortical regions but also inhibited more easily the conduction of such amygdaloid seizure discharge to the thalamus than that to the hypothalamus, subthalamus, and mesencephalic tegmentum.

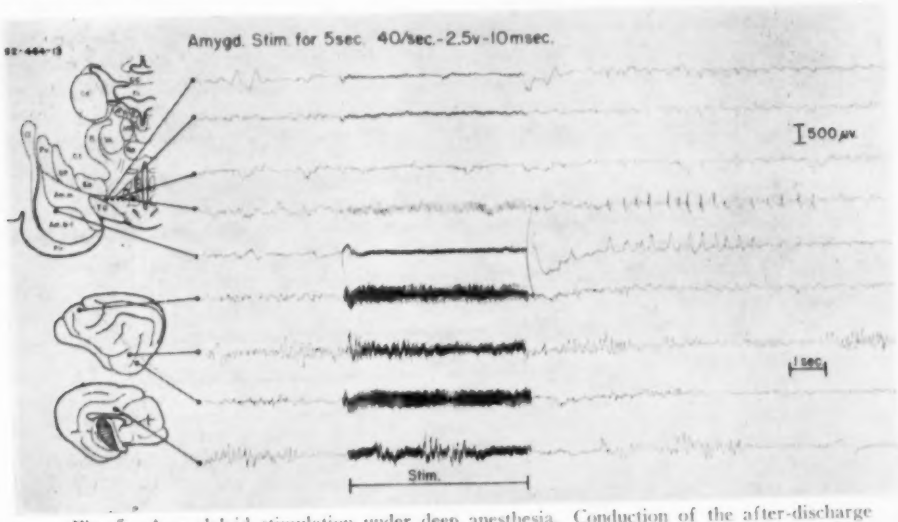



Fig. 5.—Amygdaloid stimulation under deep anesthesia. Conduction of the after-discharge to the anterior hypothalamus; no conduction to the cortex. (Lines 7, 8, and 9 are from stimulations subsequent to that seen in Lines 1-6. These subsequent stimulations produced after-discharges in the amygdala and hypothalamus identical with those seen in Lines 1-5.)

Usually the conducted after-discharge stopped synchronously with the arrest of the pacemaker after-discharge in the amygdala. Only very occasionally was there a self-sustained after-discharge outlasting the initiating discharge in the amygdala. Such self-sustained seizure discharges were recorded on one occasion in the superior lateral part of the thalamus, where the reticular nucleus covers the lateral nuclear complex of the thalamus, and at another time in the mesencephalic tegmentum. It is our belief that only such self-sustained after-discharge could truly be called a spreading amygdaloid after-discharge. In most instances in our experiment there was no true spread in the sense that an autonomous seizure discharge was induced in areas to which the amygdaloid after-discharge was conducted. This was clearly evidenced by the fact that the conducted discharge stopped simultaneously with the pacemaker after-discharge in the amygdala. Moreover, the frequency and general morphological features of the conducted after-discharge were usually the same as those of the initiating amygdaloid seizure discharge.

No constant morphological pattern of the amygdaloid after-discharge and of the conducted after-discharge was seen. A fairly frequent feature, as in human seizure discharge originating in this region, was a suppressor type of onset, where the after-discharge was preceded by a flattening of the record, merging into a slow build-up of a rhythmical after-discharge, as seen in Figure 6. Often, however, this pattern of onset was not observed, possibly because it was hidden in the stimulation artifact. Some cases showed atypical spike-and-wave complexes of 2- or 6-cps frequency. Thalamic after-discharges sometimes showed a preponderance of the slow-wave component of the after-discharge when there were signs of fatigue, whereas before this exhaustion and after recovery there was predominance of the spike component.

## Comment

The reported series of experiments represents an experimental approach in the laboratory animal to test Penfield's[9] hypothesis that seizure discharges originating in the amygdaloid region and clinically characterized by behavioral automatism are propagated from the amygdala into the centrencephalic system located in subcortical structures.

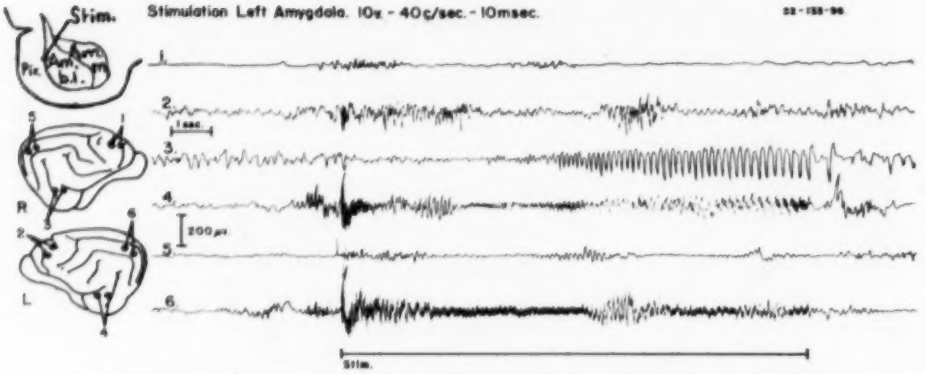



Fig. 6.—"Bitemporal" after-discharge produced by amygdaloid stimulation, showing onset with flattening of the record ("suppressor onset"). This is especially well seen on the side contralateral to the site of stimulation, where the record is free of stimulation artifact.

Figure 7 summarizes in a diagrammatic way the results obtained in this study and points out the preferential pathways of conduction of amygdaloid seizure discharge as revealed in these animal experiments. It seems from this that amygdaloid seizure discharge is most constantly conducted to ipsilateral septal, hypothalamic, and tegmental regions, and it is with the normal functions of these areas that amygdaloid epileptic discharge will therefore interfere most predominantly. Next most frequently involved is the thalamus. A somewhat less intimate relationship exists with the homolateral "temporoinsular" cortex, and still more labile is that to the contralateral amygdala. The least constant firing is that into the contralateral "temporoinsular" cortex. This demonstrates that the amygdala is indeed in most intimate relationship with those subcortical structures of integrative character which we like to consider as very important parts of the centrencephalic system, as conceived by Penfield.[9] In this respect it might be of interest to mention observations by Gastaut and associates,[14] who demonstrated that seizure discharges originating from the same subcortical areas to which amygdaloid after-discharges project by preference may be reflected in the temporal lobe, and the clinical pattern of these seizures is described as being of "psychomotor" type.

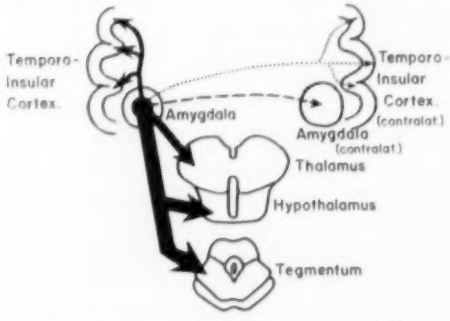



Fig. 7.—Diagram showing preferential pathways of conduction of amygdaloid after-discharge.

On the basis of our neuroanatomical knowledge of amygdaloid connections, the diffuse thalamic involvement in amygdaloid seizure discharge, affecting both specific and nonspecific thalamic nuclei, is rather surprising and difficult to understand. Some recent electrophysiological studies on the amygdaloid projection system by Gloor [16,17] may help to explain the mechanism of this diffuse subcortical propagation of amygdaloid seizure activity. These studies showed that neither single shock nor repetitive stimulation of the amygdala was able to fire the thalamus except for a quite restricted part of its diffuse projection system. The subcortical projection field of the amygdala appeared as a multisynaptic neuronal system occupying the very same areas, which

in the present study appeared as those most constantly fired by an amygdaloid seizure discharge, i. e., the septal, basal diencephalic, and mesencephalic tegmental areas.

It has also been shown in previous studies [16,17] that the subcortical amygdaloid projection field is a complexly organized agglomeration of neurons with highly flexible functional properties apt to show a prominent increase of their excitatory state under the influence of repetitive amygdaloid bombardment, as evidenced by prominent recruitment and potentiation * effects occurring in response to repetitive amygdaloid stimulation.

Moreover, potential mechanisms of reinforcement of excitation are given by convergence of alternative paths upon common neuronal pools. This is made possible by the existence of direct and indirect amygdalohypothalamic and/or amygdalotegmental pathways, some of them being relayed through an intra-amygdaloid association system and others through the powerful amplification system of the hippocampus discharging into the subcortex via the fornix.[16,17] All of these pathways share widely overlapping projection areas with the "direct" amygdaloid projection system. In view of this arrangement, and of the high sensitivity of this system to repetitive amygdaloid firing, it is easy to imagine that under conditions of epileptic discharge, where presumably the amygdala fires at or near maximal intensity, facilitation in these basal diencephalic areas may become such that the discharging process may invade the thalamus. This would explain why liminal after-discharges may fire only the basal diencephalic areas and fail to invade the thalamus, whereas slightly more vigorous after-discharges are very easily conducted into the thalamus.

This tentative explanation given for the diffuse subcortical conduction of amygdaloid after-discharges is supported by the restricted character of cortical conduction of such seizure activity, for the electrophysiological studies referred to above [16,17] demonstrated that in the temporal neocortex no prominent build-up of an increased excitatory state in response to repetitive amygdaloid stimulation takes place. Only the paleo- and archicortex (piriform cortex and hippocampus), which seem to have little if any direct influence upon the neocortical mantle, behaved like the subcortical structures. The discrete electrophysiological mechanisms allowing the extensive subcortical conduction might, therefore, not operate at the neocortical level, and this may be the reason for the lack of any extensive neocortical conduction of amygdaloid seizure activity. The present study has shown, indeed, that it is possible for the amygdala to fire into the subcortex without any neocortical after-discharge being recorded. This would be in agreement with findings reported by Brazier and associates [18] in humans where cortical electrodes over the temporal lobe at times remained silent, while deep electrodes implanted into the amygdala showed active after-discharge set up by electrical stimulation. Clinical electroencephalographers are also familiar with those cases of ictal automatism in which, during such an automatic episode, the routine EEG, even over temporal regions, remains silent or shows only some flattening, as reported by Jasper, Pertuiset, and Flanigin [5] and Gastaut and associates,[14] whereas presumably discharge originating in the amygdala actively fires into subcortical areas. Electrographic studies of such cases on the exposed temporal lobe, especially when carried out with depth electrodes introduced into the amygdala, will often disclose the origin of the patient's attacks in the amygdaloid region.

* Recruitment is meant to describe a progressive increase in amplitude of the response occurring during repetitive stimulation. It signals a progressive increase of the number of firing neurons and may also go along with increased repetitive firing of single neurons. Potentiation is meant to describe a state of facilitation outlasting the end of repetitive stimulation and is characterized by an increased amplitude of the response to single-shock stimulation applied after the end of repetitive stimulation, as compared with responses to single shocks applied before repetitive stimulation.

The neocortical topography of conduction of amygdaloid after-discharge as revealed in this study is in accordance with results reported by Gastaut, Naquet, and Roger[19] and with the experience gained in clinical electroencephalography and in electrocorticography in man. It is mostly in the anterior and mesial temporal region that we find sporadic epileptogenic potentials and seizure discharges, when the main focus is localized in the amygdala or its immediate surroundings.[2-5,11-14]

Quite interesting in respect to clinical electroencephalography is that conduction to the homologous structures of the contralateral side, i. e., the contralateral amygdala and the overlying temporoinsular cortex, was not as common and easy to obtain in our experiments in the cat as might be expected in view of the frequent occurrence of bilateral temporal discharge in human temporal lobe epilepsy. The subcortical conduction, even to the thalamus, was a more easily obtained way of propagation than that to the contralateral temporal region. Whether or not the same is true of the human brain is, of course, uncertain. It is also quite possible that in epileptics the chronic firing of a deep temporal focus may finally succeed in breaking down some barriers against contralateral spread and may finally induce the development of a secondary focus on the contralateral side. These, of course, are possibilities on which our experiments throw no light.

The inconstant firing into the anterior limbic cortex seen in some of our experiments is reminiscent of some cases encountered in clinical electroencephalography, where there seems to be an intimate relationship between mesial temporal and parasagittal epileptogenic foci. This question of interrelationship of deep temporal structures and the limbic region would, however, require more extensive experimental studies.

Our findings concerning the preferential pathways of conduction of amygdaloid after-discharge are at variance with those reported by Faeth, Walker, and Andy,[20] who describe a preferential route to the contralateral amygdala and hippocampus, followed by ipsilateral temporal cortex, hypothalamus, thalamus, caudate nucleus, putamen, and, finally, frontal granular cortex. A possible explanation for these discrepancies may be that the structures stimulated in both series were not strictly identical, since Faeth, Walker, and Andy speak of stimulation of the "amygdala-hippocampus complex," suggesting that their stimulations involved not only the amygdala but the neighboring hippocampus as well. In another point, however, there is perfect agreement between our findings and theirs; both studies show a very widespread propagation of amygdaloid after-discharge in the subcortex.

This tendency to diffuse subcortical propagation may be a general characteristic of rhinencephalic seizure discharge, since Green and Shimamoto[21] also describe a diffuse subcortical conduction of hippocampal after-discharge. With hippocampal after-discharges there was, however, a tendency to diffuse cortical involvement as well.

In view of some findings in clinical electroencephalography, the morphology of amygdaloid after-discharges as recorded in our experiments is of some interest. It was noted that many start out with a flattening of the record. This is also quite often observed in clinical cases of temporal lobe epilepsy when the patient goes into ictal automatism, as described by Jasper and Daly[22]; Jasper, Pertuiset, and Flanigin,[5] and Gastaut and associates.[14] Sometimes this flattening is even the only detectable seizure manifestation. More frequently, however, it is followed by a rhythmical build-up of synchronous discharge, as seen in our animal experiments. In some cases this flattening is generalized, involving the whole cortex. This raises the question as to whether there is any connection between this "suppressor onset" and the diffuse, low-voltage activity which can be produced by amygdaloid stimulation as first demonstrated by Kaada,[23] later confirmed by Feindel and Gloor,[24] and which the latter authors like to homologize with the activa-

tion pattern as produced by brain stem reticular stimulation.

In conclusion, we may say that epileptic discharge in the amygdala, though not necessarily disturbing cortical activity a great deal, with the exception of a relatively small area in the homolateral anteromesial temporal and insular region, may create considerable epileptic disturbance in the subcortex from the septal area back through the whole diencephalon to the upper brain stem and affecting mostly the parts responsible for highly integrative nervous processes, as postulated for the centrencephalic system. In view of these findings, the features of epileptic automatism characterized by the interference with complex integrative mechanisms of the nervous system, as supposedly depending upon the subcortical centrencephalic system, may be understood more clearly.

## Summary

The conduction of electrical after-discharge induced by electrical stimulation of the amygdaloid nucleus was studied in 19 cats in order to understand the functional anatomy of seizure mechanisms in ictal temporal lobe automatism in man known to be dependent upon epileptic discharge originating in the amygdaloid region. The findings are as follows:

1. The subcortical structures fired by amygdaloid after-discharges extend from the septal area back to the mesencephalon, with inclusion of the whole diencephalon, hypothalamus, and thalamus as well.

2. There is a rather sharp contrast between the diffuse and extensive subcortical conduction of amygdaloid seizure discharge and the restricted conduction to cortical regions.

3. The cortical areas fired by amygdaloid after-discharges comprise the hippocampus and those cortical areas of the cat's brain that are homologous to man's anterior temporal and insular cortex. These findings in the cat are in agreement with the topographical distribution of epileptic discharges in patients with ictal automatism due to discharge in the amygdaloid region.

4. Amygdaloid after-discharges are preferentially conducted to subcortical structures. Among these subcortical structures, the most constant firing occurs in the basal diencephalic and mesencephalic tegmental areas, the same regions which, on the basis of previous experiments, are known to represent the direct subcortical projection fields of the amygdala.

The mechanism of propagation of amygdaloid after-discharges to the thalamus may be related to the marked build-up of an excitatory state occurring in response to repetitive amygdaloid firing, which in cases of intense amygdaloid discharge, as in seizure activity, may supposedly become vigorous enough to allow propagation of discharge from the basal diencephalon and the brain stem into the thalamic gray matter.

The conduction to the ipsilateral "temporoinsular" cortex is more labile than that to the thalamus, and even more labile seems to be that to the contralateral amygdala and the contralateral temporoinsular cortex.

The preferential conduction of amygdaloid after-discharge into highly integrative formations of the subcortex tends to corroborate Penfield's hypothesis that the phenomena of ictal epileptic automatism may be explained on the basis that seizure discharge originating in the amygdala actively fires into the "centrencephalic system."

The frequent electrographic suppressor onset of temporal lobe seizures originating in the amygdaloid region was reduplicated in some of these animal experiments. Its possible relationship with the generalized cortical low-voltage activity, as often produced by amygdaloid stimulation, is discussed.

Dr. H. H. Jasper gave guidance and constructive criticism; Miss Mary I. Roach, technical assistance; Mrs. M. Heymann and Mrs. W. Kozicka stained and mounted the histological preparations, and Mr. Charles Hodge did the photographic work.

## Addendum

Since this article was completed, an experimental study dealing with the

same subject has been published.[25] The results and general conclusions given by these authors are in all essential points the same as those reported by us in the present study.

3801 University St. (2).

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# Sites of Origin of Hypoglycemic Seizures in the Rabbit

TOSHIHIKO TOKIZANE, M.D., and CHARLES H. SAWYER, Ph.D., Los Angeles

## Introduction

Hypoglycemia exerts profound effects on the nervous system, eventually leading to coma, which may be accompanied by seizures or convulsions. For more than 20 years insulin shock has been widely used therapeutically in the treatment of mental disorders (Himwich,[1] Kalinowsky and Hoch[2]). Although empirical in rationale, the treatment, like electroshock therapy, has been rewarded with sufficient success to make its mechanism of action worthy of study, even though the new tranquilizing agents have largely replaced it in therapy.

Numerous attempts have been made, employing the techniques of pathology and electroencephalography (EEG), to determine whether insulin therapy has a primary focus of action in the brain, with which might be correlated its beneficial effects. The pathological studies have sought the locus of lesions following hypoglycemic attacks of natural or experimental hyperinsulin origin. In addition to the cerebral and cerebellar cortices in which most authors describe marked changes, profound subcortical damage has been observed in the basal ganglia and the hippocampus (Stief and Tokay,[3] Lawrence and associates,[4] and Hicks[5]). Several authors have maintained that convulsions are necessary to produce the pathological changes encountered (see Lawrence and associates[4] for references).

From the earliest EEG studies on the problem there were indications that hypoglycemic convulsions might be subcortical in origin. Moruzzi[6] and Goodwin and associates[7,8] observed that cortical electrical activity in the rabbit was very slow and depressed in amplitude at the time of onset of seizures. Hoagland and associates[9] reported high-amplitude slow activity in the hypothalamus of the dog at a time of extreme hypoglycemic depression of the cortex. The changes were not, however, accompanied by apparent convulsions. The voluminous clinical studies on this subject have been reviewed recently by Engel and associates.[10] Even more recently, Gibbs and Murray[11] reported on three patients and concluded that in some cases of hypoglycemic convulsions the primary discharge may be cortical.

In view of this lack of agreement and knowledge as to precisely where hypoglycemic seizures originate and in consideration of the possible practical value of having this information, the present investigation was undertaken to determine the sites of origin and projection of these convulsions. The results indicate that hypoglycemic electrical* seizures in the rabbit invariably originate in and may remain locally confined to the amygdala or the hippocampus.

## Materials and Methods

Twenty-four large female New Zealand rabbits, ranging in weight from 3.0 to 4.4 kg., were employed.

In order to avoid variations attributable to dif-

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From the Department of Anatomy, University of California School of Medicine at Los Angeles, and Medical Research Programs, Veterans Administration Hospital, Long Beach, Calif.

* "Electrical seizures," as used here and subsequently, may be defined as the appearance in the EEG of electrical potentials characteristic of clinical epileptic phenomena.

ferent degrees of estrus, each rabbit received two subcutaneous injections of estradiol benzoate U. S. P.† (0.08 mg. each) during the two days preceding insulin treatment. The rabbits were also fasted from 24 to 48 hours before treatment.

The animals were prepared under ether and local procaine anesthesia for EEG recording. A tracheal cannula was inserted, but neither artificial respiration nor curare immobilization was ordinarily used, because of the hyperglycemic action of the latter (Goodwin and associates[7]). The head was fixed in a stereotaxic instrument, and deep electrodes were placed according to the atlas of Sawyer and associates.[18] Electrode sites were subsequently confirmed by histological methods.

Blood for sugar determinations was taken from an ear vein or a small saphenous vein before and after surgery and before and at periodic intervals after insulin administration. Blood glucose was assayed by the method of Mendel, Kemp, and Myers.[18] Crystalline insulin was injected intravenously, subcutaneously, and intraperitoneally in divided doses.

The splanchnic nerves were severed a week or two before insulin treatment in five rabbits. With a ventral abdominal approach the left splanchnic nerve was cut not far cephalad to the left adrenal. The right nerve was approached on the left of the inferior vena cava, which was retracted slightly to the right to protect it.

## Results

Electrical seizures were observed in 10 of 24 rabbits treated with insulin while EEG recordings were being taken. In 8 of the 10 animals undergoing seizures the blood sugar level was depressed to below 50 mg. per 100 cc. at or near the time of the seizure. In only 2 of the other 14 rabbits, which failed to exhibit seizures, was the blood sugar lowered to less than 50 mg. per 100 cc., in spite of massive doses of insulin in several cases.

Doses of insulin, in some instances up to 2000 units, failed to reduce the blood glucose level or to induce seizures. The cases in which hypoglycemia and seizures were achieved, including the splanchnicectomy series (see below), received an average of about 1000 units. In the animals in which they occurred, seizures were encountered between one and four hours after insulin treatment. Probably some others would have experienced seizures had the recording period been extended beyond four hours.

There was a suggestion of a seasonal variation in the ease with which hypoglycemia could be induced. Lowered blood sugars and seizures were readily obtained with insulin during the warm summer and fall months. Of the 14 animals which failed to show hypoglycemic seizures, 12 were studied during the cool months, from November through March. On the premise that the failure might be attributable to adrenal medullary function counteracting the effect of insulin, the splanchnic nerves to the adrenals were cut. In the splanchnicectomy series four out of five cases revealed hypoglycemic seizures; the fifth rabbit was pregnant.

Ordinarily the surgical procedures elevated the blood sugar level from about 100 to about 150 mg. per 100 cc. before recording was started and insulin was administered. This postsurgery hyperglycemia was, to a less degree, also observed in the splanchnicectomized animals. It was especially high (450 mg. per 100 cc.) in one of the two curarized preparations, tending to confirm the hyperglycemic action of curare (Goodwin and associates[7]). The other curarized rabbit responded to insulin with hypoglycemia and seizures.

The onset, progress, localization, and projection of representative hypoglycemic seizures in five different rabbits are illustrated in the Figures. The approximate blood sugar level, in milligrams per 100 cc., and time, in minutes, since the first insulin injection are given in each case. The commonly observed slowing of the EEG after treatment with insulin was confirmed, but will not be discussed further in the paper.

Figure 1 shows a seizure confined to the amygdala. The first evidence of seizure activity had been spiking in Channel 6 within an hour after insulin treatment. Several times during the next two hours there had been one-minute episodes of very fast activity, followed by spikes or

†Estradiol benzoate U. S. P. was supplied by the Schering Corporation, Bloomfield, N. J.

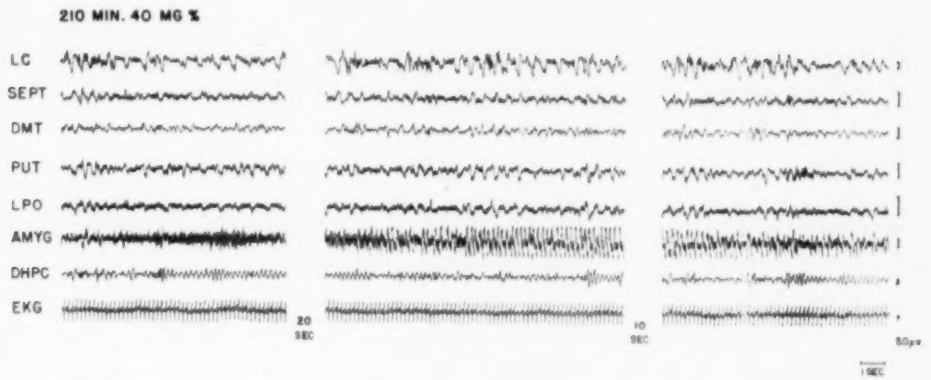


Fig. 1.—Hypoglycemic seizure confined to amygdala. Abbreviations employed in this and in subsequent Figures are as follows: *AMYG*, amygdala; *APVT*, anterior paraventricular thalamic nucleus; *CG*, central gray matter; *CL*, claustrum; *DHPC*, dorsal hippocampus; *DMT*, dorsomedial thalamic nucleus; *EKG*, electrocardiogram; *FC*, frontal cortex; *LC*, limbic cortex; *LHA*, lateral hypothalamic area; *LPO*, lateral preoptic area; *MPO*, medial preoptic area; *NA*, nucleus accumbens; *OB*, olfactory bulb; *PUT*, putamen; *RF*, reticular formation; *SEPT*, septum; *SO*, supraoptic nucleus; *SN*, substantia nigra; *STH*, subthalamus; *VHPC*, ventral hippocampus.

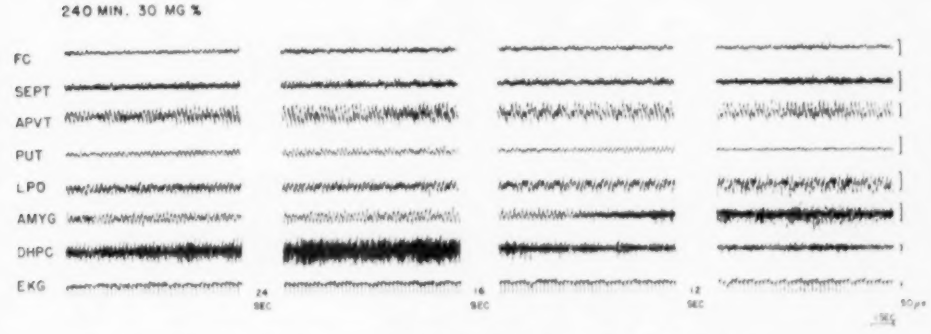


Fig. 2.—Hypoglycemic seizure involving dorsal hippocampus and amygdala.

spikes and domes in this one channel. The Figure shows a sequence of the rapid and spike-dome seizure activity. During the course of two additional hours this sequence was repeated six times, never leaving the amygdala. The blood sugar level remained at about 40 mg. per 100 cc. during this period, even though more insulin was given in an attempt to extend the scope of the seizure activity.

Figure 2 illustrates a seizure sequence involving only the dorsal hippocampus and the amygdala. Somewhat earlier in the day this rabbit had had two episodes of hypoglycemic seizure activity involving only the amygdala. The animal died some minutes after the time of this record in spite of injecting dextrose a few minutes before death.

Figure 3 shows some of the regions to which hippocampal seizures may project. The dorsal hippocampal seizure in Figure 3*A*, which is seen to involve the limbic cortex several seconds after its inception, was preceded by considerable spiking in the ventral hippocampus adjacent to the amygdala. Two minutes later (Fig. 3*B*) fast seizure activity was in progress in the ventral hippocampus and projecting to the supraoptic nucleus and, to less degrees, to

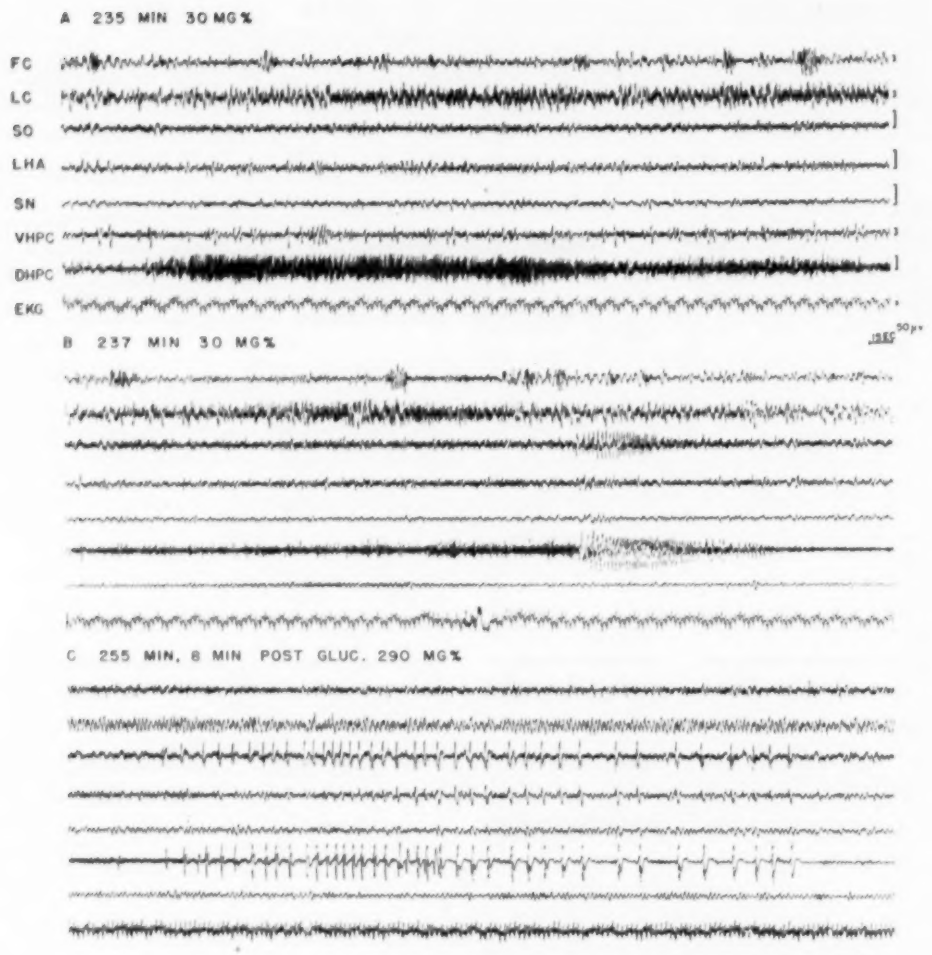


Fig. 3.—Hypoglycemic seizure arising in dorsal hippocampus and progressing to various subcortical centers, as well as projecting to the limbic cortex. See text.

the limbic cortex and lateral hypothalamic area. A movement artifact is evident in the EKG record. Twenty minutes later, or eight minutes after injecting 20 ml. of 50% dextrose intravenously, the blood sugar level registered at 290 mg. per 100 cc. (Fig. 3C). At this time, during the process of recovery, spike-dome seizure activity in the ventral hippocampus is seen projecting to the supraoptic nucleus and the lateral hypothalamic area. The other channels show electrical records characteristic of the alert rabbit.

Four minutes before the beginning of the record contained in Figure 4, the rabbit jerked and initiated a localized dorsal hippocampal seizure, apparently by mechanical stimulation. Figure 4 illustrates the progress and projection of an amygdaloid seizure during postseizure depression in the dorsal hippocampus. It is apparent that projections from the amygdala activate spikes in the medial preoptic, subthalamic, and reticular formation areas, but especially are they prominent in the lateral hypothalamic

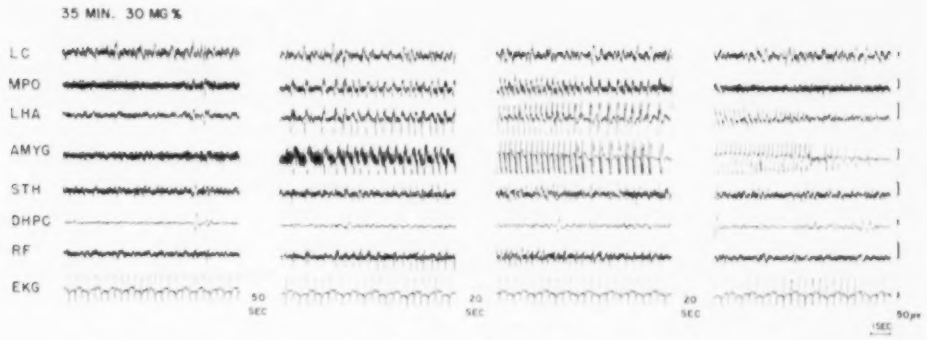


Fig. 4.—Characteristics and sites of projection of an amygdaloid seizure which occurred during postseizure depression in the dorsal hippocampus.

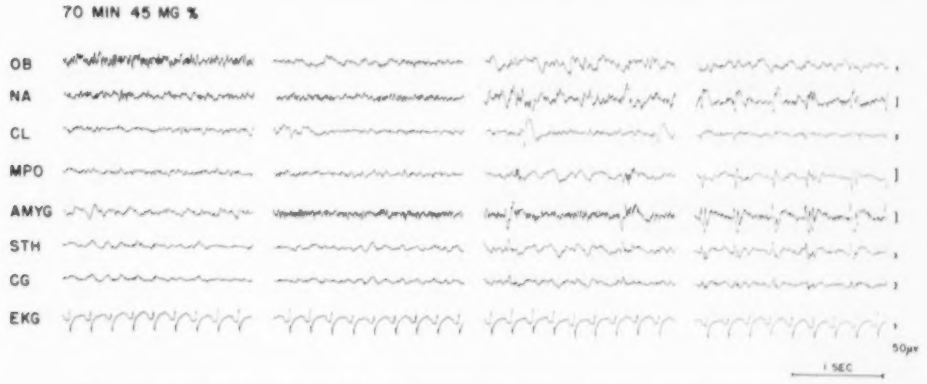


Fig. 5.—Amygdaloid seizure and its projections seen at faster paper speed.

area. Indicative of their origin, the spikes in the amygdala outlast the projected spikes in other channels.

Figure 5 illustrates an hypoglycemic amygdaloid seizure and its projections at faster paper speed. The seizure is seen to arise with fast (50/sec.) activity exclusively localized in the amygdala. It then proceeds to break into spike-dome bursts, which become more frequent and project especially to the nucleus accumbens and medial preoptic and subthalamic areas. At this paper speed it is apparent that the amygdaloid spikes precede their counterparts in at least some of the other channels.

The last animal (Fig. 5) was a curarized preparation; all of the other nine hypoglycemic seizure rabbits, including the four whose recordings are shown above, were noncurarized, essentially unanesthetized (except for local procaine), but restrained animals. Movement artifacts were not uncommon, but they were much less likely during the localized electrical seizures than before or after this period. In most cases there was no external sign of seizure activity beyond mydriasis.

## Comment

The amygdala and hippocampus have certain distinctive features which may at least partially explain their supersensitivity to hypoglycemia. When the blood sugar is depressed, there is no reason to suppose that these regions receive any less sugar than the rest of the brain, but it appears that their thresholds to hypoglycemia are lower. Among their other unusual features

are (1) the high amplitude of the electrical waves in their resting EEG records (see calibration in the Figures); (2) the low threshold for the induction of seizures on electrical stimulation of the amygdala (Gastaut and associates[14]) or the hippocampus (Green and Shimamoto,[15] Liberson and Akert[16]); (3) their low seizure threshold to treatment with cholinergic drugs (MacLean and Delgado[17]) or hypertonic saline (Sawyer and Gernandt[18]); (4) the fact that over one-half of all the focal epilespsies seem to start in the amygdala (Jasper[19]), and (5) the close anatomical and functional relations of both hippocampus and amygdala with the hypothalamus and visceral activity (Gastaut[20]; Green and Arduini[21]), which often finds expression in psychomotor seizures.

Seizures in the dorsal hippocampus tended to remain sharply confined there or to progress slowly (minutes) to the ventral hippocampus and amygdala. From the ventral hippocampus or amygdala they either remained localized or projected principally to the preoptic, septal, hypothalamic, subthalamic, and midbrain tegmental nuclei. Not unless the seizure was quite severe did it involve the cortex or cause motor symptoms easily discerned. This projection pattern agrees closely with amygdaloid seizure projections in the cat described recently by Gloor,[22] Naquet,[23] and Arana-Iniguez and associates.[24] It would seem highly probable that such seizures could occur but remain undetected during insulin coma therapy in the absence of EEG recording, and possibly even if cortical EEG records were taken. In view of these considerations, the hypoglycemic seizure records of Gibbs and Murray[11] mentioned earlier would appear to represent the cortical projection of amygdaloid or hippocampal seizures.

The brief period of subcortical seizure activity shortly after dextrose administration in Figure 3 deserves comment. It may be that in this case, and in one other responding similarly, the blood sugar level dropped below the point which would sustain seizure activity; hence, a brief seizure occurred during the recovery phase. Holmberg[25] has commented on a critical blood sugar level to sustain seizure activity in electroshock therapy.

There is disagreement in the literature as to whether seizures are necessary for the hypoglycemic production of brain lesions (Lawrence and associates[4]). The commonness of cortical lesions would tend to deny it, but, in view of our results and the extremely severe nature of the lesions described in "Ammon's horn" (Stief and Tokay,[3] Lawrence and associates[4]), it seems likely that seizures may be related to the pathology of hyperinsulinism.

If amygdaloid or hippocampal stimuli or lesions, evoked or produced by hypoglycemic or electroshock seizures, constitute the key reaction on which the beneficial results of shock therapy depend, it would seem desirable to exploit this reaction directly and avoid the less desirable side-effects of the treatment. Preliminary results of stimulating and making lesions in the amygdaloid complex of human epileptic patients have been reported by Chapman and colleagues.[26] They observed changes of blood pressure, heart rate, and pupillary dilatation, visceral effects such as had been seen earlier in lower forms. Attempts to apply localized deep electrical stimulation of other parts of the human brain in problems of mental illness have been made by Heath and others.[27] Such approaches should be made with extreme caution under the most carefully controlled conditions (Lilly[28]), but it is to be hoped that localized nondebilitating therapy in mental disease may hold promise for the future.

Quite recently MacLean and co-workers[29] have reported the results of experiments in cats in which reserpine treatment induced behavioral changes similar to those evidenced during hippocampal seizures. Furthermore, reserpine treatment and insulin seizures had similar effects on protein synthesis by the brain. Still more recently, chlorpromazine has been reported to produce

isolated seizure activity in the amygdaloid nuclear complex of the intact unanesthetized cat.[39] Thus, it would appear that the newer pharmacological treatments of mental disease may exert profound effects on the same subcortical centers preferentially affected by insulin coma—the hippocampal-amygdaloid limbic system.

## Summary

An electroencephalographic study has been made of the characteristics, sites of origin, and projection of hypoglycemic seizures in the restrained, noncurarized rabbit. Records were made of the electrical activity of the cerebral cortex and subcortical centers approached by stereotaxic means. The results reveal that insulin-induced hypoglycemic seizures arise in and may be confined to the amygdala and/or the hippocampus. Severer seizures may project to the preoptic, hypothalamic, and other brain stem regions without reaching the frontal or limbic cortical area. The localized seizures are not accompanied by any apparent somatic motor activity and are detected only by the deep electrodes. Increased secretion of adrenaline following surgery and stereotaxic restraint may counteract the effect of quite massive doses of insulin to the extent that the blood sugar level is not lowered to the seizure range. The adrenal effect may be counteracted by cutting the splanchnic nerves. It is suggested that the beneficial results of insulin therapy may be related to undetected subcortical seizures.

Mrs. Ruth Shull made blood sugar determinations; Miss Cora Rucker prepared brains for histological study; Mr. Charles Bridgman lettered the Figures, and Mr. Timothy Dodge photographed them.

Department of Anatomy, University of California School of Medicine, Los Angeles (24).

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# Antidiuretic Effect of Lysergic Acid Diethylamide in Humans

**MARIAN W. KIES, Ph.D.; DALE HORST; EDWARD V. EVARTS, M.D., and NORMAN P. GOLDSTEIN, M.D.,**
**Bethesda, Md.**

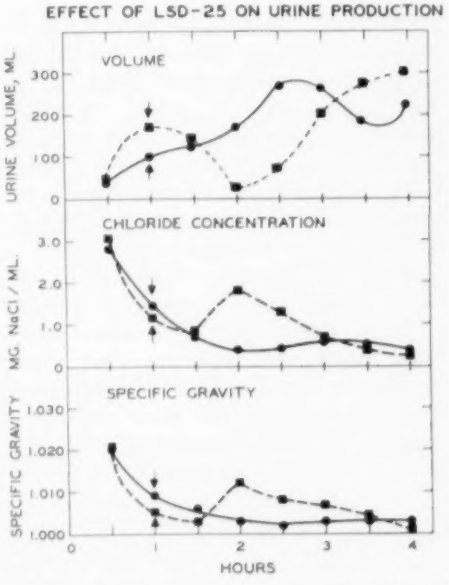
In the years following the first clinical report on the effects of lysergic acid diethylamide[1] many publications have described both the psychological and the physiological alterations produced in human subjects by LSD. Although its site of action has not been established, there has been considerable speculation that some of the psychological effects of LSD are related to hypothalamic stimulation. Since one effect of hypothalamic stimulation is increased production of antidiuretic hormone,[2] the assumption that LSD acts by stimulating the hypothalamus would carry the prediction that LSD should have antidiuretic properties. The data to be described demonstrate that LSD has strong antidiuretic effects; these data are consistent with the notion that hypothalamic stimulation may be related to certain of the psychological effects of LSD.

## Experimental Study

The subjects were seven healthy male subjects, ranging in age from 19 to 29 years, who were given lysergic acid diethylamide in connection with psychological studies made in our laboratory. No food was given after 8 o'clock on the evening before each experimental period, although water was allowed ad libitum. At 8 a. m. on the day of an experiment the bladder was emptied and 500 ml. of tap water was ingested. Thereafter, the bladder was emptied and 200 ml. of water administered every half-hour until the end of the four-hour experimental period. One hour after the beginning of the experiment the subjects were given an intravenous injection of 100γ of LSD-25 in 1 ml. of saline or a placebo of 1 ml. of saline. The subjects were instructed to sit quietly, or recline, with a minimum of muscular exertion.

The urine volumes for each half-hour period were measured and the chloride concentration determined by the Volhard-Harvey method, as described in Hawk, Oser, and Summerson.[3] There were 19 control experiments and 14 experiments in which subjects received LSD-25.

The effect of the intravenous LSD-25 on the urine volume of hydrated subjects is shown in the Figure. There is a marked antidiuresis, which is apparent one hour




Effect of intravenous injection of lysergic acid diethylamide (LSD-25) on urine volume, chloride concentration, and specific gravity in hydrated human subject. Arrows indicate time of injection of either 1 ml. of isotonic saline (solid lines) or 100γ of LSD-25 in 1 ml. of isotonic saline (broken lines).

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Dr. Goldstein's present address: Mayo Clinic, Rochester, Minn.

National Institute of Mental Health, National Institutes of Health, Public Health Service, U. S. Department of Health, Education, and Welfare.

after the injection of the LSD-25 and which lasts for one hour. Later, there is an increased urine output as compared with the corresponding control periods. Although there was considerable variation in both the control values and the individual responses to the drugs, the antidiuretic effect of LSD-25 during the fourth and fifth collection periods (one and one and one-half hours after administration) was highly significant ($P = < 0.01$). The subsequent increase in urine production of the subjects receiving LSD-25 was significantly different from the controls only during the eighth period.

LSD also exerts an effect on the urine chloride concentration. Although LSD did not significantly alter the total chloride excretion, the effect of the drug was evident in the increased chloride content of the urine voided one to one and one-half hours after injection.

## Comment

The mechanism whereby the administration of LSD-25 in hydrated subjects produces an antidiuretic effect is not known. One may speculate, however, that this physiological response to LSD-25 is the result of antidiuretic hormone (ADH) liberation which follows hypothalamic stimulation by LSD. The pattern of urine suppression, with corresponding increase in chloride concentration, is similar to the effects of anoxic painful stimuli in man observed by Kelsall [4] and Mirsky and Stein.[5] These authors used a physical stress which they believed stimulated the hypothalamus to release increased amounts of the antidiuretic hormone. In our experiments, LSD-25 may have constituted a chemical stress. There is one important difference between the antidiuretic effects of painful stimuli and those of LSD. In the experiments reported here the antidiuretic response to LSD was considerably delayed (more than one-half hour), whereas the antidiuretic response to physical stress reported by Mirsky and others was apparent within 10 minutes. This delay in the antidiuretic response to LSD is in contrast to the psychic effects of the drug, which in these subjects were demonstrable in 5 to 10 minutes. It may be that the hypothalamic stimulation postulated is itself a secondary effect, arising from the effects of LSD-25 on other central nervous system structures.

Erspamer [6] has shown that the antidiuretic effects of serotonin in the rat are inhibited by LSD. This antidiuresis is explained by Rothlin et al.[7] in terms of the effect of serotonin on renal blood flow. Although LSD has no marked effect on renal blood flow under the specific experimental conditions cited, it inhibits the action of serotonin. It should be pointed out that the antidiuresis reported here is dissimilar to the antidiuretic action of serotonin and that there is no inconsistency in the two reports.

## Summary

LSD administered to hydrated male adults exerts a marked antidiuretic action, which begins approximately one-half hour after intravenous injection of the drug and whose duration is roughly one hour. Thereafter, an increased urine output compensates for the excess water retained by the body during the antidiuresis. It is suggested that this effect of LSD may be the result of hypothalamic stimulation, although the experimental data do not exclude other possible explanations.

Laboratory of Clinical Science, National Institute of Mental Health.

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# Society Transactions

## BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Nov. 17, 1955

DR. ERICH LINDEMANN, M.D., President, Presiding

**Neuropathology of Experimental Pyridoxine Deficiency.** DR. MAURICE VICTOR and DR. RAYMOND D. ADAMS.

The purpose of this study is to report the neuropathologic findings in pyridoxine-deprived monkeys. Six monkeys were made deficient by withholding pyridoxine and were compared with a similar group of monkeys on stock rations. One additional monkey was rendered deficient by the administration of desoxypyridoxine. The most readily discerned abnormality was in the cells of Betz and, to a less pronounced extent, in the smaller pyramidal cells of the cortex. The affected cells appeared swollen and rounder than usual, with eccentric nuclei and varying degrees of loss of the Nissl particles. In some monkeys there was a slight increase in the astrocytic glia. The brain stem, cerebellum, spinal cord, dorsal root ganglia, and anterior and posterior roots showed no consistent lesions. The peripheral nerves were affected in all but one of the deficient animals. In general, the nerve affection was slight, being greater in the sciatic than in the brachial nerves. In the desoxypyridoxine-treated monkey the nerve lesion was very severe. In none of the sections did the blood vessels appear abnormal. The control animals showed no significant neuropathologic changes.

The changes in the cells of Betz were similar, though not identical with those seen in pellagra.

### Discussion

DR. RANDOLPH K. BYERS: I wonder if any pyridoxine diets were fed young monkeys. We have seen babies with convulsions controlled after the baby was placed on a pyridoxine diet.

DR. JOSEPH M. FOLEY: Were there any vascular changes, such as have been described by some in pyridoxine deficiency, especially in the smaller blood vessels? Did any of these animals have convulsions? Has the work progressed to a point where it is possible to define what is going on in the cell? What is the nature of the cytoplasmic disintegration? At what point is the process reversible?

DR. ROBERT S. SCHWAB: How many months or weeks can the monkeys go on this diet and then return to a normal diet and no change be found?

DR. D. DENNY-BROWN: How do Dr. Victor and Dr. Adams exclude the possibility of the effects of general malnutrition in experiments lasting more than 200 days? Does not the poor gain in weight mean the operation of secondary factors? Further, thin, sick monkeys tend to sit on their haunches for long periods and thus develop pressure lesions of the sciatic nerve. Was the peripheral degeneration found in other nerves? The affected nerve cells shown seemed to me to have a darker, more homogeneous cytoplasm than those seen in pellagra.

DR. CHARLES A. KANE: Once the animals were rendered deficient, was replacement made orally or by injection?

DR. JOSEPH M. FOLEY: I notice that Dr. Victor discounts the significance of the dark-staining nerve cells. Although they are seen with some regularity in routine pathological material, they are, nevertheless, different from the usual appearance of the nerve cell. Is it possible they mean something other than artifact?

DR. ERICH LINDEMANN: I was impressed by the amount of generalized nutritional state. I was not clear whether that happened in spite of the same caloric intake.

DR. MAURICE VICTOR: As to Dr. Byer's question whether baby monkeys had fits, I do not know whether such an experimental study has been done; I doubt it. One pediatrician has put two babies on a pyridoxine diet. He claims both these children had had convulsions.

In regard to the vessels of the brain, we looked carefully for vessel change but could not find any. Two separate groups of investigators, Rhinehart and Greenburg, and Musbett and Emerson, at Merck & Co., have both studied the blood vessel change carefully. They have been unable to find any involvement of carotid and cerebral arteries. The blood vessel change has been produced in dogs, as well as in monkeys.

Could we have missed some convulsions through a lack of continuous supervision? We may have. As it is, we saw convulsions in one pyridoxine-deficient monkey, and, interestingly, these occurred only after pyridoxine therapy was reinstituted.

The question whether the nerve cell changes represented are an axonal reaction cannot be settled with finality. We feel that the change could not suitably be called an axonal reaction, for the reason given before. There are no nuclear inclusion bodies seen.

We did try to reverse the pathologic changes by giving pyridoxine to the deficient monkeys. In one monkey, pyridoxine was given after 105 days of deficiency—intravenously, intramuscularly, and by mouth, without complete reversal of the changes. Some changes we illustrated were from monkeys treated with pyridoxine after a prolonged deficiency period. Both, however, had been deficient for a long time before treatment was reinstituted.

We feel there is a difference between the appearance of the Betz-cell cytoplasm in the pyridoxine-deficient monkeys and that in pellagrous patients. It is difficult to describe the difference in words. Brachial nerves were affected, as well as the sciatic nerve, although to a less pronounced degree.

DR. RAYMOND D. ADAMS: I do not know how one can get at this problem of controlling other nutritional factors involved in animal experimentation that covers a long period of time. The proof as to whether the changes produced were purely due to pyridoxine deficiency would come from a reversal of the pathologic changes by the administration of pyridoxine (vitamin $B_6$). Even that might not clinch it for the changes may be irreversible. If animals get no pyridoxine, they become sickly. If they show enough inanition, they do not develop vitamin deficiency. It was almost impossible to produce symptoms of pyridoxine deficiency in the dogs which would have died if the vitamin had not been given. These are problems confronting everyone working in the nutritional field.

Dr. Victor asked about the cell change. At first I was loath to accept this as a significant pathologic finding, since three or four animals died during the night and were autopsied the next morning. We wondered whether this was a postmortem artifact, but it is an unusual type of change for a postmortem artifact.

Dr. Foley asked what we thought was going on in the cell. I doubt whether our stains are good enough to settle that at the moment. We haven't done the stains for intranuclear inclusions. If the change we saw is a reliable one, something has happened to the nuclear metabolism of the cell whereby chromatolysis occurs, at first in the perinuclear zone. I do not attach any significance to the spike cell. That is frequently a postmortem artifact. In the European literature, it has been recorded that simply tapping the spinal cord will increase the number of spike cells. They were found in all our experimental material, and they have no meaning here. All of us are aware of the mistakes that have been made in regard to this cell. It has been presented as the earliest change in anoxia, which it certainly could not be.

We used Marchi stains. They did not help us very much.

**Treatment of Parkinson's Disease: A. Psychotherapy in Parkinson's Disease.**
DR. MORRIS E. CHAFETZ.

Emotional upsets intensify the symptoms of Parkinson's disease. An attempt was made to utilize group and individual psychotherapy as a means of understanding the emotional reactions and improving the adjustment to this disease.

There was no specific pattern of response, although a number of mechanisms predominated. Denial was a prominent and common feature. It appeared in response to anxiety over what the illness had done to the patient's self-sufficiency. Inability to perform everyday functions easily led to exaggerated feelings of helplessness. These feelings of helplessness served to intensify fears of dependency.

Since the patients have a conspicuous illness, denial did not work completely, resulting in varying degrees of depression. The more the patient was depressed, the more he tended not to follow his medication schedules carefully. This resulted in an uneven response to treatment, which, in turn, increased the depression, thereby establishing a vicious cycle.

In patients with obsessive-compulsive-like personality structures, the slowness caused by Parkinson's disease interfered with their ritualistic defense system. This resulted in anxiety

over primitive impulses, which cannot be as successfully defended. This anxiety is further heightened when increased efforts to reestablish predisease patterns failed.

Treatment by the group technique was effected by (1) universalization of patients' problems, (2) development of group cohesiveness, (3) lessening of social isolation, and (4) intragroup support. In the individual therapy setting, support is effected by (1) reestablishing successful defense patterns, (2) active support in attempts to maintain healthy, independent relationships, (3) working through aspects of dependency fears, and (4) classification of misconceptions concerning the disease.

Of the patients seen, approximately one-half (60) accepted further psychiatric interviews. From this group, two-thirds (40) were benefited.

**B. Five-Year Report on Drug Therapy.** Dr. Robert S. Schwab and Eleanore K. Garvey.

With the introduction of new synthetic drugs that have some antirigidity and antitremor effects in Parkinson's disease, a rather confusing picture has been created as to what are the best preparations. This report is an assessment of the relative efficiency of eight preparations that have been in use for the past five years.

In 1949 a relative comparison of the effectiveness of these drugs was made at the International Neurological Meeting, and the order of effectiveness was as follows:

| Drug | No. Still on Drug | Total | Per Cent |
|---|---|---|---|
| Artane | 59 | 75 | 78 |
| Panparnit | 54 | 87 | 64 |
| Benadryl | 44 | 72 | 61 |
| Solanaceous | 72 | 157 | 46 |
| Phenergan | 6 | 14 | 43 |
| Thephorin | 13 | 41 | 22 |
| Amphetamine | 11 | 36 | 31 |
| Parsidol | 6 | 25 | 24 |

At the present time this has been reexamined and the order is as follows:

| Drug | No. Still on Drug | Total | Per Cent |
|---|---|---|---|
| Parsidol | 163 | 243 | 67 |
| Thephorin | 140 | 308 | 45 |
| Artane | 131 | 298 | 44 |
| Benadryl | 57 | 170 | 33 |
| Amphetamine | 56 | 190 | 29 |
| Panparnit | 14 | 91 | 15 |
| Solanaceous drugs | 17 | 186 | 9 |
| Phenergan | 1 | 17 | 6 |

The index of each drug is determined by the number of patients that have been given the drug during the past five years divided by the number still taking the drug when the present assessment was made. For example, 163 of 243 patients are still taking Parsidol, as opposed to 131 still taking Artane out of a total of 298.

Newer drugs, such as Pagitane and Kemadrin, have not been available long enough to be compared with the above preparations but seem to be running about the same as Artane. The use of amphetamines and other analeptics has greatly helped some patients in tolerating effective therapeutic doses of the other substances.

The shift from the Artane and solanaceous drugs may be due in part to the shift in the age distribution of the Parkinson population, from a peak in the 50- to 59-year age group to that of the 60- to 69-year group. For example, in 1948, among 252 patients there were 10 under 29 years of age; 43 in the 30- to 39-year group; 62 in the 40- to 49-year group; 77 in the 50- to 59-year group; 53 in the 60- to 69-year group, and only 7 over 70. In contrast to this, our present population (October, 1955) consists of 331 patients distributed as follows, with the peak a decade higher than in 1948: 0 under 29 years of age; 28 in the 30- to 39-year group; 48 in the 40- to 49-year group; 82 in the 50- to 59-year group; 114 in the 60- to 69-year group, and 59 over 70.

It is well known that the side-effects of the atropine drugs increase with advancing years.

### Discussion on Articles by Drs. Chafetz and Schwab

Dr. Benjamin Simon: There are a number of interesting features in the psychological situation of Parkinsonism which is not true of many other organic disorders. In Parkinsonism the psychologic effects are often manifest before there is knowledge of the neurological dis-

order. One of the earliest becomes apparent in the sexual life of the patient. He becomes awkward. His rigidity has not yet become marked, and there seems to be no explanation. In illness in general there is a state of dependency which tends to intensify empathy. In Parkinsonism the dependency is a repellent type, leading to rejection rather than to acceptance. Group therapy, in this situation, presents some interesting aspects. On the surface, Dr. Chafetz' presentation would seem to present a good argument for homogeneity of groups. This I would dispute. Ulcer patients whom I once treated identified with each other as positives on the basis of their disorder and presented a broad front to society. Treatment was very difficult until the group was broken up and mixed with other types of emotional disorders. In Parkinsonism, the identification produced a group unity on the basis of a definite and perceptive physical disorder. They are able to meet the aggressor with a common front. I do not believe this would have been true if the Parkinson cases had been mixed with others. In these cases exposition of subtle dynamics was obviously useless. Instead of trying to deal with narcissism for the establishment of better object relationship, in Parkinsonism we replace the repelling objects with objects similar to each other, and which are in empathy with each other.

Dr. Henry R. Viets: There is hardly any other disease with more marked clinical signs than Parkinsonism. One of the reasons many patients are depressed is based on their mental alertness, even after their facial expression is lost. To friends and neighbors, a mask-like face, postural immobility, and tremor indicate "failure," both bodily and mental. Facial expression is the sort of thing cartoonists emphasize. Certain expressions are signs of success. It is said that no public figure can be a famous politician without certain facial characteristics. The Parkinsonian, keenly alert, may think in terms of public approval, and this may be the main reason in a few instances for his abnormal mental state. How difficult it is to judge a patient's mentality when no facial expression is shown! Dr. Denny-Brown will remember the rigid, expressionless Sir Henry Head in the last years of his life. In spite of his symptoms, he was all too keenly alive to his situation, and depression was brushed aside by his magnanimous outlook on life. But many patients need psychotherapy on a level of normal mentality in an environment of grave physical disability. To differentiate between dullness of expression and dullness of mind is one of the secrets of successful care of the Parkinsonian.

Dr. Erich Lindemann: While both these topics were discussed, I wondered about the use of the word therapy with respect to a disease process. The word psychotherapy is often used to denote systematic efforts to alter psychological processes when the disease is primarily a psychological disorder. We have in Parkinsonism a progressive brain condition impairing posture and motility, and we have a certain psychological response. I wonder if it would not be more appropriate to think of the management of psychological sequelae as something different from what we ordinarily call psychotherapy. I think that was implied in Dr. Viets' remark— whether internist, neurologist, or psychiatrist is likely to be familiar with dealing in a human way with the consequences of an illness. It might be good to separate them a little from what we usually call psychotherapy.

Dr. Morris E. Chafetz: In ulcer patients the disease entity is not observable to the environment. However, in Parkinson's disease, it is not only observable, but prominent, thereby creating different emotional stress situations. With the use of the group technique, we only hoped to effect a means of increased support to these patients and we were leaving deeper dynamic structures alone. Thereby, we pursued group therapy with limited goals. In the individual therapy sessions, a more classical therapeutic approach was made, with the goal of achieving insight and altering significantly the patients' behavior. Naturally, in the limited time, I was unable to report on the dynamics evolved in the individual psychotherapeutic setting. I should like to say to Dr. Viets that not all the patients we saw were depressed. Others had developed other emotionally incapacitating syndromes, which were probably present premorbidly, but which became overt with the development of Parkinsonism. Another point: patients who develop a conspicuous disease, like Parkinsonism, are confronted with emotional traumata that have a different meaning to each patient, and these must be worked out psychotherapeutically.

Dr. Robert S. Schwab: Can the ordinary doctor give a depression psychotherapy? I always thought I could. I have been disturbed in my naïvette, encouraging the patients with support which fails to help. Then a psychiatrist takes over and does not concern himself with medicine. Much to my surprise, the depression lifts. Whether one really needs two people separately attacking their problems, we cannot be sure.

**Mental Health Film and Group Psychotherapy.** MR. SAUL COOPER and DR. MERTON J. KAHNE.

An interdisciplinary project involving the departments of nursing, physical medicine and rehabilitation, psychology, and psychiatry of the Boston VA Hospital was developed around the exploratory use of mental health films in a group setting. During a period of one year, 20 closed-ward patients were shown and given an opportunity to discuss 39 films. The experiences of the group were assessed in terms of (1) the interplay of specific effects called out by the films with those due to the processes of a formal psychotherapeutic group, (2) the safety of using mental health films with severely emotionally disturbed people, (3) possibilities of education of such patients to general principles underlying modern mental health concepts and psychiatric practices, (4) the influence of such a program on hospital policy and functioning.

It was found that the films had a marked catalytic effect on the group process. The procedure complemented and tended to facilitate other therapeutic procedures. With adequate communication between participant and nonparticipant personnel, realistic decision making and assignment of responsibility, and psychotherapeutic supervision, the procedure was safe. Transitory disturbances did occur but could be used to the patients' clear benefit. Patients used relatively little jargon and few clichés, caught on to why the therapists were interested in their biographies, and seemed to achieve wider knowledge of human behavior and greater understanding of the common roots of different reactive characteristics of people. There was an indirect educational effect on nonparticipant personnel, increased use of audiovisual aids in the training programs, and formation of another, more purely educational, film group. There was also some concern about the advisability of censorship of nonmental health films being shown to the general medical and surgical patients (nonpsychiatric) in the hospital.

### Discussion

DR. ERICH LINDEMANN: This very interesting review of a group experience is open for discussion. I have been wondering whether the fact that they were mental health films was an important issue. Perhaps having a film of Peter Pan, or H. S. Pulham, Esq., might also initiate an interesting group discussion in which increased communication, sharing of experience, group cohesion, and joint consideration of the mastery of life problems might result. There must be something about these so-called mental health films which might be interesting to discuss further.

DR. WILFRED BLOOMBERG: A few points are worthy of further comment. I would like to remind the audience that the patients here described and discussed were all closed-ward patients, though this has not been stated in the paper. It is interesting that the work started with a concern about the problem of showing or not showing certain films to psychotic patients. Our VA Central Office has a department which screens films and decides whether they are suitable for psychiatric patients or not. In our decentralized lack of wisdom in our hospital, we have questioned the judgment of this screening department. We think that there may be a basis for censorship of films, but that the department doing it had not yet discovered the proper basis. Our patients have not been disturbed by Westerns with lots of shooting. The only picture which so far has disturbed them was a fantasy science-fiction one that got in by mistake, that portrayed unpleasant things, and that the staff found just as disturbing as did the patients.

A second point of interest brought up by this paper, although it is tangential to the purpose of the patient group, is that it clearly points up the fact that when these films are used in mental health education, they should not be sent out for showing without a competent discussion leader to go along with them. Unless there was such a discussion, each person who saw the film saw something so different in it from the others that the film could well be meaningless for basic educational purposes.

I wish the film makers would listen to papers like this. I have had some experience with people who make documentary films. They find a psychiatrist and list him as a consultant. They talk over a good topic and ask for a good example from clinical material. They ask if this is a sound way to do it. Then they say goodby and never see the psychiatrist again. They write the script, and they make the films with the notion that they are the ones that know about making the films and that they need no further help. I have tried to get film makers to submit some of their films for criticism to intelligent, but unsophisticated, audiences, but have had very little success. An example was a film of several years ago which showed

a patient being brought back to a hospital screaming and being hustled by three aides down a corridor. We knew, and the film makers knew, that this was a temporary relapse and that the patient would get better. However, this was not made clear in the film, and the makers were not even interested in finding out what a lay audience would think on seeing such a scene portrayed.

I have been fascinated in watching the experience reported here and have been impressed by the courage of the group who started it. I am pleased with the results.

DR. BENJAMIN SIMON: Let me carry the idea a bit further with the example of "Let There Be Light," a documentary film in which there are no "artifacts," and which I have been using for some time in the treatment of patients. I have found that the closer the film gets to the patient's experience the more it disturbs him. I do not mind this, since it is a focus around which therapy can be developed. When the film is shown to psychotics and psychoneurotics, they generally react as did Cooper's patients. When shown to veterans in general, we get the same reaction, but when shown to male veterans who have been treated in the service for psychoneuroses, we get a much more disturbed response. Interestingly, this is not seen in officers or female veterans with neuroses. The film is a film of military psychoneurotics in the military service. Since it is absolutely documentary, the identification would appear to be too intense.

I was interested in the idea of the theoretical basis for the efficacy of films presented by Mr. Cooper. I agree that the film acts as a screen for the projection of the inner tensions. A good psychiatric film has the same value as a good painting for the projection of primary process phenomena—visual, imagery, condensation, displacement, etc. When the film is artificial and tends to be didactic, there is litle reaction and less therapeutic reaction.

DR. MARTHA BRUNNER-ORNE: We found the use of educational films very helpful in the treatment of alcoholics, particularly when followed by discussions. I remember one film which was extremely successful. The film was called "Alcohol and the Human Body." It demonstrates the physiology and metabolism of alcohol and shows how alcohol is broken down in the organism. The film demonstrates how alcohol attacks the nervous system first. In a simple way, by means of animated drawings, it points out that the frontal lobes are affected immediately.

After the film was shown and the physiology of the frontal lobes was discussed, somebody brought up the point that this film offered a good explanation why people did not stick to their good intentions of having one or two drinks only, i.e., because the judgment and planning centers were affected. Long after this film demonstration, with the following discussion, I had many reverberations from participants in the meeting. Even though not quite scientifically valid, it had an extreme impact on the people present, and it was amazing to see how much benefit was derived.

We hope to have more good films in the field of alcoholism, although I don't think it is necessary to present films with alcoholism as the only topic. We are planning to use psychological films in the treatment of alcoholics and also in our general reeducation endeavors.

DR. MERTON KAHNE: I want to thank the people who have discussed the paper. I think Dr. Simon is correct. I want to emphasize one aspect: the general notion that runs around psychiatric circles, that it does not make any difference what you say, but it matters how you say it. We showed many of the films in this series to psychiatric personnel of our hospital. They all had ideas that they were not made well and were not good. Our patients had almost the opposite response, the intensity being in direct proportion to the degree of illness. As they got better, their attitudes were closer to those of the personnel, and they were more critical about technique. As to Dr. Lindemann's question whether it matters whether or not this was a mental health film: I think it does make a difference. They were talking very directly about feelings of depression; about lobotomy for schizophrenia. Not only was there an effect in psychotherapy, but problems relating to apprehension about electric shock therapy were discussed in greater detail. They were talking about very specific things. The interesting thing to us was the use of films related to normal or abnormal childhood development. Patients were very interested in these films, and that played an important part in the second year of work. This project started with an observation about a fear, common in mental hospitals, of exposing patients to anything strongly emotional. One evening a group of disturbed patients was supposed to see a boxing bout on television. The bout was canceled, but a film, "Schizophrenia," was shown instead. These very disturbed patients responded with rapt attention. They were quiet and asked questions the next day. They were interested in the problem. None were disturbed by the experience. The

apprehension that goes around hospitals is more in the personnel than in the patients. If these films are used, there should be ample time for discussion, and there must be continuity in the group. If the patients do not have the support of a large group, they will leave, get upset, and the therapy can leave negative effects. Once the group process begins to have an effect, the films can be used with a remarkable degree of success.

## PHILADELPHIA NEUROLOGICAL SOCIETY

ERNEST A. SPIEGEL, M.D., Presiding

Regular Meeting, Feb. 3, 1956

**Epidermoid Tumors of the Ventricles: A Report of Two Cases.** Dr. Michael Scott.

Two cases of epidermoid tumor or cholesteatoma of the ventricles were reported. The first case was that in a young woman who complained primarily of loss of vision in the right eye for a period of three years, before her present admission to the hospital. She also had a history of having had generalized convulsions, preceded by an epigastric aura and associated with a "far-away feeling," for 20 years. These convulsions had been absent, however, for the past seven years. The neurological examination showed optic atrophy in the right eye, an inferior temporal quadrant cut in the left eye, and only a small island of vision in the right eye. The remainder of the neurological examination was negative. The air encephalogram revealed a tumor in the right lateral ventricle and beneath the third ventricle. These air studies were typical of those described by others as specific for epidermoid or cholesteatomatous tumors of the ventricles. At operation a huge cholesteatoma was found in the right lateral ventricle, and an extension of the tumor was found from the tip of the right temporal horn lateralward and near the chiasm, but apparently outside the third ventricle. This small extension of tissue had a capsule, which was partially removed. No attempt was made to do a complete removal of the portion of the tumor beneath the third ventricle because of the site of the lesion and the lateral approach for the surgery. Microscopy showed epidermoid tumor. Recheck examination made six months later revealed a patient in excellent health but with no improvement in vision. The second case is that of a middle-aged woman who had classical symptoms of cerebellar involvement associated with choked disc and dysmetria, ataxia, and hypotonia of the left upper extremity. At operation a large encapsulated epidermoid tumor was found in the fourth ventricle. The entire tumor, together with its capsule, was removed. The tumor contents were unusual in that there were small collections of cholesteatomatous material, which actually resembled small pearls within the tumor. Microscopy revealed epidermoid tumor. Recheck examination five years later showed an excellent recovery except for minimal signs of left cerebellar involvement. These cases will be reported in full in a subsequent publication.

### Discussion

Dr. G. M. Austin Jr.: Dr. Scott is to be congratulated for his skillful technical operation on the two patients. He has given us a clean-cut review of the literature. In a large series of brain tumors 1.5% are epidermoids. These are avascular tumors, usually very easy to remove. Removal of the tumor from the fourth ventricle was a nice achievement. Epidermoids are infrequently seen in the cerebellopontine angle, with the capsule usually densely attached to the dura and to the 9th and 10th cranial nerves, making complete removal difficult in this location.

Dr. J. Rudolph Jaeger: Dr. Scott's presentation of epidermoid tumors has been well done. In my experience these lesions occur in almost any part of the cranial cavity. I can distinctly recall that several have been removed from the third and lateral ventricles, and also from the fourth ventricle. The common location is in the cerebellopontine angle. At least three were causing tic douloureux, and a fourth one in this location had been diagnosed as an acoustic neurinoma. Perhaps they are less common on the outer cortex of the cerebral hemisphere. I recall one at the base, against the third cranial nerve. Two others were in the motor cortex near the midline; one of them was associated with a tremendous degenerated cyst surrounding it, which had caused a sudden hemiplegia. Apparently these tumors differ in their general consistency and surrounding reactions, depending on their location within the cranial cavity. Fortunately, they are benign and easily removed in almost every instance.

**Sciatica in Amputated Legs.** Dr. Arthur B. King.

Two cases of protruding intervertebral discs in the lumbar region are described. Both men had had major amputations of a lower extremity sometime before the onset of symptoms referable to the protruding discs. Neither had any complaints that suggested the so-called

phantom limb phenomena. Both had sciatica with complaints of pain extending into the missing lower leg, foot, and toes. The description of the pain was just as exact as in patients who had their lower extremities intact. Removal of the offending disc relieved the symptoms completely. There was no trouble in diagnosing the protruding disc, despite the absence of portions of the lower limb, which removed the possibility of objective signs, such as loss of ankle jerk, weakness of motion of the toes, and sensory losses in the lower leg and foot. The straight-leg-raising test was positive when applied to the stump. The observation was made that, despite the loss of a peripheral portion of the sciatic nerve, the root apparently remains intact and functioning for at least 27 years after removal of the leg and that the special pattern of pain remained intact.

### Discussion

DR. ROBERT A. GROFF: Dr. King is to be congratulated on discovering another cause of phantom limb pain. It seems reasonable that a herniation of the nucleus pulposus can develop in patients with an amputated leg. "Sciatica" as a term annoys me because it includes so many possible conditions. A herniated nucleus pulposus causes root pain and not sciatica. For this reason I would suggest that Dr. King change the title of his paper to "Root Pain in Amputated Legs Caused by Herniated Discs."

DR. MICHAEL SCOTT: Dr. King's presentation demonstrates that patients with phantom pain should have myelograms done more frequently. Dr. H. Wycis had a similar case of phantom sciatica due to a herniated disc. Occasionally referred pain to the lower extremity may be caused by a high thoracic tumor. I have recently reported five such cases.

DR. ARTHUR B. KING: The whole topic of phantom limb is confusing from both the psychiatric and the neurological standpoint. I also have had several cases with pain in the lower limbs from high thoracic lesions. The present cases had nothing to suggest phantom limb pain.

**Bilateral Facial Palsy and Peripheral Nerve Involvement Presenting Signs of Bronchogenic Carcinoma.** DRS. GEORGE D. GAMMON, GERALDINE KING, and GABRIEL SCHWARZ.

The case report of a 41-year-old man admitted with bilateral facial paralysis and weakness of both lower extremities was presented. A Guillain-Barré syndrome was suspected; the true diagnosis of bronchogenic carcinoma with central nervous system metastasis was not apparent until eight months later. The spinal fluid findings of a protein of 115 mg. per 100 cc.; 50 red cells and 60 white cells per cubic millimeter, colloidal mastic curve of 0143332100, and negative studies other than evidence of severe degeneration of the seventh nerves by electrical tests were felt confirmatory. The condition, however, progressed, with evidence of spinal cord involvement and, later, involvement of other cranial nerves including the 3rd, 8th, 9th, and 10th bilaterally. Chest x-ray, eight months after initial symptoms, showed an area of pulmonary condensation. Repeated spinal fluid examinations showed elevated cell counts, high protein, and, when specifically examined, low sugar values. However, the fluid was negative for bacteria and fungi. (The chloride values were somewhat lower than normal.) Autopsy, performed after an illness of one year's duration, showed bronchogenic carcinoma with diffuse meningeal carcinomatosis. There was invasion of cranial nerves and spinal roots by the carcinoma cells. There were metastases within the cord itself in the cervical region, and smaller nests in the thoracic and lumbar areas, as well as demyelination of the posterior columns and the anterolateral tracts of the cord.

### Discussion

DR. MATTHEW T. MOORE: The authors are to be congratulated on this unique case presentation. In a recent survey of 18 cases of metastatic malignancy to the nervous system, I found 7 which were of bronchogenic origin. One case showed metastasis to the spinal cord in which the clinical syndrome was similar to the case presented, in that the features of the Guillain-Barré syndrome were present early in the clinical course. The metastatic lesion involved the fourth thoracic segment. Study of the chest had disclosed negative findings; yet at autopsy a bronchogenic carcinoma the size of a lemon was found. X-ray studies of the chest may be unreliable in carcinoma of the lung. If such a lesion is suspected, repeat studies are advisable. In another case, that of a man who was admitted to a state hospital, with the diagnosis of undifferentiated psychosis, x-rays of the chest were interpreted as showing diffuse pulmonary tuberculosis of the right lung. Autopsy disclosed carcinoma of the lung with diffuse metastasis to the brain and meninges. In my series, 50% of the cases of metastatic bronchogenic carcinoma disclosed negative chest x-rays.

DR. AXEL K. OLSEN: I would like to ask whether any stained specimens of the spinal fluid were done? We had one case some months ago which demonstrated lymphoma cells in the spinal fluid. The patient died a few months later with markedly enlarged mediastinal nodes.

DR. DAVID J. LAFIA: Metastatic bronchogenic carcinoma may present bizarre clinical pictures. I recall one patient studied by arteriography because of subarachnoid hemorrhage. Autopsy disclosed bronchogenic metastasis in the cerebellopontine angle. The other case showed a mixture of shoulder girdle atrophy and hemiplegia.

DR. LAWRENCE J. BARROWS: A number of cases of carcinomatous spread to the spinal cord and cranial nerves have been missed because of incomplete microscopic examinations. We recently had a case of a lymphoma in which the cauda equina appeared normal grossly but tumor cells were found in the microscopic sections. It has been pointed out by others that this is also frequently the case in lymphoepitheliomas of the nasopharynx. We have another case in the laboratory in which gross lesions were demonstrated at autopsy on the third, fourth, and seventh cranial nerves; in this case the neurological symptoms were the presenting manifestations of a carcinoma of the sigmoid colon which remained undiagnosed during life.

DR. ARTHUR B. KING: I reported 100 cases of carcinoma of the lung and described cases of tumor meningitis. In one case the diagnosis was made by spinning the cells down in the spinal fluid. One should always think of metastases in cases of meningitis of obscure origin.

DR. GABRIEL A. SCHWARZ: This case again illustrates the fact that the nervous system can be involved before the signs of the lung carcinoma become manifest. It again emphasizes the necessity of taking chest x-rays as a routine procedure in all neurological cases. One of the procedures that might have been used on this case would have been to centrifuge cerebrospinal fluid and attempt to find carcinoma cells in the fluid. There is another possible procedure of diagnostic value which might be used in some of these cases. The spinal fluid might be centrifuged and concentrated, and the material might then be injected into the aqueous humor of a guinea pig in the hope that if carcinoma cells were present, they might grow out, and then possibly microscopic examination would give a more definitive diagnosis.

DR. GEORGE D. GAMMON: The reason for reporting this case lay in the confusion in diagnosis and the long course of the metastatic lesion before it was possible to discover the original source in the lung. The pathological findings indicate carcinomatous involvement of cranial nerves and of roots lower down. It is not clear whether the latter could account for the demyelination of the posterior columns or whether this represents the systemic effects of the carcinoma, independent of actual direct involvement. In addition, there appears to be an intraspinal metastasis, which is a rarity.

DR. ERNEST A. SPIEGEL: About 30 years ago Dr. T. Démétriades studied in the Vienna Neurological Institute the Nissl structure of cells in the brain stem in cases of extracerebral malignant tumors. He found definite degenerative changes in the cochlear and other nuclei apparently caused by metabolic effects of the tumors.

DR. MATTHEW T. MOORE: I would like to ask Dr. Schwarz if he has any ideas as to the route of dissemination in this case.

DR. GABRIEL A. SCHWARZ: Dr. Moore's question of the method of dissemination in this case must necessarily remain highly theoretical. In this particular case, it seems to me that the spread was first to the subarachnoid space, and then a secondary invasion of the central nervous system itself. I make this suggestion because the initial symptoms were facial palsy and then sometime later there developed the weakness of the lower extremities. Actually, the cord signs did not appear for quite a period of time after these initial symptoms. This would suggest that the original involvement was the subarachnoid space, and thence an invasion of the spinal cord. It has been generally assumed that intracerebral carcinomatous metastases occur by the hematogenous route. It had been suggested previously that meningitis carcinomatosa was due to transport of the carcinoma cells by means of the lymphatics. However, Batson's observations of the venous system of the spinal column have helped to explain the vascular venous metastasis and could well explain the process in our case.

## PHILADELPHIA PSYCHIATRIC SOCIETY
**JOHN E. DAVIS, M.D., Presiding**
**Regular Meeting, Feb. 10, 1956**

**Recent Studies in Psychopharmacology.** DR. SEYMOUR KETY, Bethesda, Md.

Accepted attitudes toward the causes of mental illness have shown wide swings in the past. Early beliefs in evil spirits gave way to materialism, where even consciousness was a secretion

of the brain. This resulted in an exclusively organic concept of mental illness, which, with the research tools then available, led to rather naïve and disappointing hypotheses. Partially in reaction to this approach, the pendulum then swung toward psychodynamic theories, recognizing the importance of experience and personal interactions and with a regrettable tendency of some of its proponents to neglect the brain altogether. The discovery and rediscovery of drugs that affect the mind now appears to be producing another swing. It is to be hoped that this last swing need not be all the way over to the biological side, to the exclusion of any other aspect, and that a new approach may emerge, recognizing, on the one hand, the importance of the brain in mental illness without neglecting the fact that this, of all organs, has the ability to learn and to be modified by past experience. A drug that acts directly upon the heart or upon the liver shows relatively little variability in its effects, as opposed to psychopharmacologic agents, the response to which represents an interaction of the drug, the brain, and the personality of the subject.

The problems involved in proper evaluation of psychotherapeutic drugs are not so great as to preclude the possibility of controlled and valid studies. A number of such studies have been done, although they are still in the minority, and these have indicated significant improvement in certain psychiatric disorders.

Equally interesting are the psychotomimetic agents, which may help to locate brain mechanisms involved in mental disease and to elucidate a biochemical basis if, indeed, one exists. Studies with mescaline and with lysergic acid diethylamide (LSD-25) have raised a number of interesting questions. Although the psychological effects of these agents have been well substantiated, the physiological or biochemical basis of their action remains to a considerable extent obscure. The relationships between mescaline and epinephrine and their degradation products have been pointed out by a number of investigators, and the interactions of LSD with serotonin and the possible role of serotonin in the nervous system are at present a challenging concept.

## Discussion

DR. HARRY PENNES: There are highly individual factors in drug reactions, both inter- and intra-individual, and variations are dependent upon a basic physiological or psychological state. Drug effects may be classed as primary, which are predictable and consistent in people and animals, and secondary, which are the varying compensatory and other reactions in response to the primary effects. It is suggested that there might be classification of personalities based upon responses to drugs. No drug regularly, in 100% of subjects, produces discrete emotional responses (anxiety or rage, etc.), and emotions are probably much more complicated reactions than any reactions produced directly by drugs.

DR. HERBERT FREED: The chlorpromazine-reserpine group of drugs modulates the fight-flight reaction of Cannon. Thus we are able to keep the patient in contact with us and facilitate the interpersonal relationship. LSD-25 often tends to elicit sufficient anxiety that the patient again enters into a psychotherapeutic relationship to lessen his tension. Thus, with either group the resultant effect is beneficial for psychotherapy. Therefore we do not need to be apprehensive that we will remove the motivation for therapy by completely removing anxiety. Chlorpromazine, which usually controls the "LSD psychoses," may be looked upon as acting both on the primitive psychomotor system (thus affecting the fight-flight reaction) and on the primitive psychosensory system. This latter system is that manifested by the varied states of consciousness, in contrast to the sensations of the classical sensory system. The hypothesis (Morison) is offered that in the psychosis, etc., these two sensory systems are out of synchronization.

DR. FRITZ A. FREYHAN, Farmhurst, Del.: I wonder if we are clinically prepared for the important developments taking place in research laboratories. Modern drug therapies are most effective in the treatment and management of psychiatric patients, most of whom are institutionalized. The past has shown that the greater number of institutions did not collect data on somatic treatments in a scientific manner. It is evident, then, that scientific progress necessitates greater psychiatric interest in mental hospitals, which have long been neglected in this regard. As to the effectiveness of neuroleptic drugs, Parkinsonism, so frequently observed during therapy, should be considered not as a side-effect but as an important psychomotor manifestation of the action of the drug upon subcortical functional centers. This is demonstrated by the fact that psychomotility and its hypernormal manifestations constitute the clinical criteria for treatment with neuroleptic drugs.

# News and Comment

## ANNOUNCEMENTS

**Clinical Investigator Program.**—The needs of the Veterans Administration Medical Program and the potential of its research and education activities in contributing to the health of the nation are such that it is planned to train selected physicians and dentists whose primary responsibility will be medical research. The candidates for this appointment must be interested in problems of particular importance in the care of veteran patients in fields basic to neurology and psychiatry, cardiovascular disease, cancer, degenerative diseases, and problems involving the aging process. Maximum freedom of choice of subject will be allowed within these broad fields.

Any physician or dentist is eligible who has completed at least the formal residency training period required prior to American Specialty Board certification and, because of special interest and aptitude, wishes to do full-time research for a period of possibly up to three years.

The Clinical Investigator will spend at least three-fourths of his time in research. The balance of his time may be spent in teaching and patient care or in whatever professional activity he and his sponsors agree is advantageous for his development. He will be appointed as a full-time member of the Veterans Administration hospital staff, and his official title will be Veterans Administration Clinical Investigator. He will be entitled to the privileges and benefits of other full-time physcians and dentists, such as insurance and retirement eligibility, and annual and sick leave. All Clinical Investigators will have research as their primary responsibility; they will, in additon, hold suitable clinical appointments on the hospital staff which will enable them to enjoy the privileges of a responsible relationship to the patient care program.

Candidate nominations are sent to the Veterans Administration hospital manager through the Veterans Administration Hospital Research Committee for approval by the Deans Committee. From the group of nominees the Clinical Investigators will be selected by the Central Advisory Committee, composed of outstanding educators and investigators.

**Psychopharmacology Service Center, National Institute of Mental Health.**—The Psychopharmacology Service Center has been established within the Research Grants and Fellowships Branch of the National Institute of Mental Health.

The purpose of the Center is to implement a broad program of basic and clinical research aimed at increasing understanding of the mechanisms of action, efficacy, and limitations of the tranquilizing and other centrally active drugs. The program of the Center includes the stimulation and support of work on the basic pharmacological and psychological mechanisms of drug action, experimental and clinical studies of drug effectiveness, and research aimed at the development of improved and new methods for predicting and evaluating the efficacy and toxicity of these compounds. The Center will perform information, research advisory, and coordinating functions, including consulting services, surveys, publication of a newsletter, and summaries and reviews of recent and on-going research.

The program of the Center will include support through the existing grant and award programs of the National Institutes of Health. These programs include research grants, research fellowships, training grants, etc. Grants will be provided for clinical and basic research, for development of methods and techniques, and for cooperative clinical trials.

The professional staff of the Center at present consists of Jonathan O. Cole, M.D., Psychiatrist, as Chief, and Sherman Ross, Ph.D., as Research Psychologist.

## GENERAL NEWS

**Publication of *Archives italiennes de biologie* Resumed.**—The *Archives italiennes de biologie* will again appear in 1957. Publication was stopped in 1935, when Professor Aducco

retired. The papers will be written in English or French, according to the choice of the author. It is the editors' hope that contributors from other countries will feel free to utilize the *Archives* as a channel of publication. Another aim of the journal will be to afford Italian investigators an outlet which will, by virtue of the language of publication, be more easily available to readers in other countries. The editor is Giuseppe Moruzzi, of the Istituto di Fisiologia della Università di Pisa, Via S. Zeno N. 11-13, Pisa, Italy.

## PERSONAL NEWS

**Dr. Robert B. Livingston Appointed Scientific Director, National Institutes of Health.**—Dr. Robert B. Livingston has been appointed Scientific Director of the combined basic research programs of the National Institute of Mental Health and the National Institute of Neurological Diseases and Blindness in Bethesda, Md. Dr. Livingston succeeds Dr. Seymour S. Kety, who has asked that he be relieved from the position of Scientific Director in order to devote full time to his own laboratory investigations in the field of cerebral blood flow.

**The American Board of Psychiatry and Neurology, Inc.**—The American Board of Psychiatry and Neurology, Inc., announces that only two examinations will be given in 1957:

New Orleans, on March 18 and 19, 1957
New York, on Dec. 16 and 17, 1957

Beginning Jan. 1, 1958, all unused examination fees, or portions of examination fees, on deposit in the Board Office will be forfeited by the candidate to the Board when the application lapses by going out of date. Further, all unused examination fees, or partial unused examination fees, deposited before the date of Jan. 1, 1952, will automatically be forfeited by the candidate to the Board on Jan. 1, 1958.

# Books

**J. M. Charcot, 1825-1893, sa vie—son œuvre.** By Georges Guillain. Price 1400 fr. Pp. 186. Mason & Cie, 120 boulevard Saint-Germain, Paris 6e, 1955.

On the first page of this biography is recorded the birth of Jean Martin Charcot to a 28-year-old carriage builder and his 16-year-old wife. On the second page he is described as a taciturn, cold, reserved, and studious youth. By the fourth page *le Maître* has reached his internship and prepared a thesis on gout. Thereafter, although this account is divided into two sections, one relating the life and the other the work of Charcot, the impression is readily developed that Charcot's life drew meaning almost entirely from his work. There prevails throughout a justified reverence for *le fondateur de la neurologie*. His exacting and comprehensive devotion to his subject, his application to both pathology and clinical experimentation, and his excellence as a teacher and physician are extolled; his limitations are explained as those imposed by the inadequacies of the available techniques and data. This appraisal does not represent the prejudice of this famous French neurologist-biographer, for it is clear from the accounts of Freud and the records of Zilboorg, among others, that Charcot's diverse talents made the Salpêtrière the mecca of world neurology.

Interwoven in the presentation of Charcot's activities are interesting anecdotes about the position of the Salpêtrière in French political and psychiatric history. For example, an administrative change separated into two groups, the psychotic patients from the hysterical and epileptic, and led to Charcot's development (and subsequent abandonment) of the concept of hysteroepilepsy. There are summaries of Charcot's vivid descriptions of tabes, multiple sclerosis, aphasic disturbances in migraine, trophic changes in extremities affected by hysterical paralysis; there is a review of Charcot's reasons for rejecting Broca's narrow view of aphasia, and there is a relatively extensive coverage of Charcot's descriptions and ideas of hysteria and hypnosis, which were his main interest in his last years. Charcot's work impressively supports his view that *les malades, eux n'ont pas changé*; it is only that the perceptions and discernment of a Charcot illuminate anew the functioning and recurrent problems of man.

**Life Stress and Essential Hypertension.** Stewart Wolf, P. V. Cardon, E. M. Shepard, and H. G. Wolff. Price, $7.50. Pp. 256. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore, 1955.

This book is one in which hypertension is viewed in the context of the lives of hypertensive patients. Variations in hemodynamics are correlated with events of significance in the life situation, and short-term situations of emotional stress are shown to be capable of altering underlying mechanisms, such as peripheral vascular resistance, renal blood flow, and blood viscosity.

The natural history of the disease has been carefully documented in 114 patients, along with changes in their life experience. Fourteen of these subjects lost all evidence of hypertension in association with learning to be less restrained and more assertive in their patterns of living. The authors are cautious not to attribute essential hypertension to any single causative agent, but they provide convincing support for the relevance of personality adjustment to the process. The book reports studies of not only essential hypertension but also other circulatory disorders in the framework of the patient's life adjustment.

The authors are members of a group of investigators which, for the past fifteen years, studying bodily changes in the precise setting of the laboratory, has been able to relate pathogenic mechanisms to the aims, goals, and adaptive problems of the individual patient. The monographs growing out of this work began with the classic study of a man with a gastric fistula, "Human Gastric Function," and have ranged through such diversified subjects as "Headache," "The Nose," and "The Human Colon."

In the present volume the authors have forged another link in the chain of evidence relating life stress to symptoms and disease. The material is well presented, and the charts and diagrams which accompany the text are pertinent and instructive. This book should be of interest to any person who deals with patients having essential hypertension and to all those who are interested in a fuller understanding of stress and disease.

SECTION ON
PSYCHIATRY

# Why Patients Leave Psychotherapy

JEROME D. FRANK, M.D.; LESTER H. GLIEDMAN, M.D.; STANLEY D. IMBER, Ph.D.; EARL H. NASH Jr., M.S., and ANTHONY R. STONE, M.S.S.W., Baltimore

## Introduction

Psychotherapy is assumed to be the treatment of choice for most psychiatric outpatients; yet the demand for it far exceeds the supply of psychotherapists. Neither the upsurge of new pharmacological agents, whose chief value in outpatient work seems to be to facilitate psychotherapy,[1] nor expanded training programs can bridge this gap in the foreseeable future. For this very practical reason, as well as for many theoretical ones, every effort must be made to deepen our understanding of the processes of psychotherapy so as to increase the efficiency of current psychotherapeutic procedures and perhaps discover more effective ones. In order to do this, a valid appraisal of current procedures is a prerequisite.

Since the response to psychotherapy depends on the interaction of a particular person with a particular situation, this appraisal can be approached from two directions. One, which has received the most attention, is to describe the attributes of the situation as carefully as possible, with a view to identifying those components which are responsible for its therapeutic effect. Although there are innumerable clinical and theoretical descriptions of various forms of psychotherapy, the methodological obstacles to obtaining objectively verifiable data about them have been formidable. Only recently does some progress appear to be made in solving these.[2,3]

The other approach to appraising psychotherapy would be from the standpoint of attributes of the patient which predispose him to respond favorably or unfavorably to different forms of treatment. That this line of attack may be fruitful is suggested by the well-known fact that about two-thirds of patients seem to improve regardless of the type of psychotherapy they have received.[4] Furthermore, the same improvement figure crops up with methods of treatment which are not labeled as psychotherapy, such as that offered by general practitioners,[5] or $CO_2$ treatment.[6] This finding suggests two obvious implications. One is that much of the therapeutic efficacy of any given form of psychotherapy depends on components which are common to all forms. These could be, for example, the conjunction of a help seeker and a help giver, who is regarded by both parties as able and willing to help, empathy of the help giver for the help seeker, and the suggestive power of the helper's conviction that his method will produce results.

The other implication of the over-all two-thirds improvement rate is that a large pro-

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From the Department of Psychiatry, The Johns Hopkins University School of Medicine.

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portion of patients respond favorably to the nonspecific components present in all forms of treatment. Thus, it seems likely that the improvement rate of any specific type of psychotherapy is made up of those patients who would improve without therapy, those who would respond to any form, and some who might be responding favorably to the characteristics which differentiate this form of therapy from others. The presence of large numbers of patients of the first two types might obscure real differences in the efficacies of different types of therapy for different types of patients.

The present report is an aspect of a larger study to determine the attributes of patients which determine their responsiveness to the presumed common features of different forms of psychotherapy.

The responsiveness of a patient to a given form of psychotherapy involves two components: his staying in treatment and his improvement under it. The first is a necessary, but not sufficient, condition for the second—a patient cannot improve under psychotherapy unless he remains in treatment. He may, however, remain in treatment and yet fail to improve under it. We believe that this distinction may have clinical as well as logical validity and shall present some preliminary data to substantiate this. The present report, however, is primarily concerned with factors determining whether or not a patient remains in treatment. We shall summarize our results and, by relating them to the findings of others, attempt to arrive at some general formulations. The problem of improvement will be considered fully in later publications.

The problem of suitability for psychotherapy has assumed major importance only with the growth of large psychiatric outpatient clinics supported in part by public or institutional funds. Private psychiatric practitioners have been chiefly interested in describing their methods of treatment. The problem of who will accept the form of treatment they offer has understandably been of little concern. Because of the investment of time and money required by private psychotherapy, the patients who reach the psychotherapist's office have already largely selected themselves as suitable for what he has to offer. Since the demand for private psychotherapy far exceeds the supply, the therapist can easily replace patients who terminate treatment. Moreover, since each psychotherapist sees relatively few patients, it is difficult for any one practitioner to accumulate a large enough sample for study. Hence writings on psychotherapy by psychiatrists have had relatively little to say about suitability for psychotherapy and do not support their statements with data.[7-11]

The situation is very different with regard to mental hygiene clinics. Since patients pay for only part of the cost of treatment and facilities are overtaxed, the question of their most efficient use becomes important. A major source of wastage is the 30% to 65% of patients who, often after quite extensive and time-consuming initial examinations, terminate treatment prematurely. The large number of patients seen and the presence on clinic staffs of persons trained in research facilitate systematic study of this problem, which is of equal interest to administrators and therapists. The study of termination of treatment has a particular methodological attraction in that termination can be clearly defined. Whatever the number of treatment sessions selected as the demarcation between terminating or remaining in treatment, it is unambiguous, in contrast to the multifaceted and controversial criterion of "improvement." It is not surprising, therefore, that an increasing number of quantitative studies carried out by clinical psychologists are appearing which attempt to clarify factors related to whether psychiatric outpatients remain in treatment or leave it prematurely.

The literature now contains reports, chiefly from Veterans Administration Mental Hygiene Clinics, covering various aspects of the termination problem, with a total of at least 2400 patients, in addition to two qualitative studies, in which the size of the sample is not specified. The three studies

having the most bearing on the present one are those of Rubinstein and Lorr,[12] Hiler,[13] and Dengrove and Kutash.[14] Since their findings are remarkably consistent with ours, and with the less detailed findings reported in the other studies, the time seems ripe for an attempt to generalize concerning some of the factors related to remaining in or leaving treatment. Rubinstein and Lorr studied 128 veterans from nine different Veterans Administration Mental Hygiene Clinics, all nonpsychotic, dichotomized into two groups. "Remainers" had been in treatment for at least six months, or a total of 26 visits; "terminators" had had 5 or less visits and had stopped against or without the advice of the therapist. The two groups were compared statistically in terms of various tests and inventories. Hiler, using a sample of 302 patients seen at one Veterans Administration Clinic, compared patients who left treatment in 5 or less sessions with those who stayed 20 sessions or more, on a battery of psychological tests. Dengrove and Kutash offer a qualitative study based on case records of veteran patients who left treatment before it was completed. Mensh and Golden[15] reviewed the records of 575 veterans at one Veterans clinic and are chiefly concerned with relation of length of treatment to improvement, as well as general statistical characteristics of the population studied. Garfield and King,[16] in a statistical study of the records of 1216 veteran patients, report primarily on the drop-out rate and the relation of length of treatment to improvement.

Five relevant studies have appeared dealing with non veteran populations. Koren and Goetzel[17] made a qualitative study of the first year of operation of the Wayne County Mental Health Clinic. Auld and Eron[18] compared Rorschach and Wechsler-Bellevue scores of patients in a psychiatric outpatient department of a general hospital who accept and reject treatment. Rickler, Klein, and Basson[19] studied 100 unselected consecutive cases who came to the offices of three psychiatrists in private practice. Rogers and Dymond, and their associates,[2] as part of their elaborate studies of psychotherapy, report on 25 patients who failed to complete six or more sessions, but the authors were chiefly interested in comparing how these patients changed as compared with those who received more treatment. Dollard and Miller[20] have a thought-provoking discussion of patient selection for psychotherapy based on learning theory.

## Description of the Study

*A. Population.*—A total of 91 patients who appeared at the Henry Phipps Psychiatric Clinic outpatient department between June, 1953, and October, 1954, were included in this study. All white patients between the ages of 18 and 55 were included, except those with organic brain disease, antisocial character disorder, alcoholism, overt psychosis, or mental deficiency. The opinion of the psychiatrist who first saw the patient in the clinic as to his suitability for psychotherapy had no bearing on whether or not a patient was accepted for the study if he met the criteria for inclusion. There were 56 white women and 35 white men, with a median age of 29.7 years. All but one were initially diagnosed as having a psychoneurotic or personality disorder, the one exception being an ambulatory schizophrenic whose disease was misdiagnosed.

*B. Design.*—Since we were primarily interested in patients' responsiveness to those aspects of psychotherapy which are common to different forms, and the qualities of the psychotherapist not unique to any one psychiatrist, it seemed desirable to include in the design more than one form of therapy and more than one psychiatrist. Three forms of therapy were chosen which could be differentiated crudely without detailed knowledge of the therapeutic process: group therapy one and one-half hours per week, individual therapy at least one hour a week, and "minimal individual therapy" not more than one-half hour every two weeks. The last-mentioned therapy was included for two reasons. First, it represents a treatment situation which approximates the theoretical ideal of a "no-treatment" control as closely as may be considered ethically feasible without the outright denial of help to a sick patient seeking treatment. Second, previous unpublished results of our research had indicated that amount of contact between therapist and patient has relevance for the success of treatment. The minimal form of treatment differs from the other two mainly in that it involves fewer and shorter contacts between patient and therapist and, therefore, affords an opportunity for validating the previous results.[21]

Three members of the psychiatric resident staff at The Johns Hopkins Hospital each conducted all three forms of treatment. Each was in the second year of his residency training and, under supervision, had treated many patients individually and had conducted at least one therapy group. Patients were randomly assigned to each therapist and therapy by the research staff. The psychiatrists and patients were urged to remain in contact for at least six months, unless the psychiatrist felt that the patient had received maximum benefit before that time. Each of the psychiatrists was assigned a roster of at least 18 patients, 6 in each of the three forms of treatment. In anticipation of early dropping out from treatment, a larger number of patients than the rosters required were initially assigned so that each therapist would be assured of treating at least 18 patients beyond the third interview, which the research staff arbitrarily set as the minimum criterion for a "therapeutic experience." Each patient, whether he stayed in treatment or not, was reevaluated six months after entering therapy, again six months later, and at yearly intervals thereafter. In most cases a relative or close friend of each patient was also interviewed separately but at approximately the same time as the patient.

*C. Description of Measures.*—Although this report is concerned primarily with data which prognosticate whether a patient will remain in or leave treatment, it seems desirable to include a brief overview of all measures used in the study. From the standpoint of the over-all project, those selected to measure improvement are basic, since the ultimate test of any therapy is the extent to which it helps patients to get better. Improvement measures are also relevant to the present report, since initial scores on them were studied as possible prognostic indicators for remaining in or leaving therapy. Selection of measures to evaluate improvement proved to be a vexing problem, which has been discussed in detail elsewhere.[8] We finally accepted the same definition of improvement that is used throughout medicine: In treating disease the physician's goal is to restore the patient to his previous level of *comfort* and *efficiency*. The same criteria were applied to psychotherapy. Comfort was defined in terms of symptoms or feelings which cause distress. Effectiveness was defined as the adequacy with which the patient manages his relations with others so as to achieve fulfillment of his desires and theirs. For methodological reasons both these variables were defined in negative terms. We tried to measure decrease in discomfort and social ineffectiveness, rather than increase in comfort and effectiveness. The rating scales for describing these dimensions were used to evaluate both initial status and change from one evaluation to the next. Other measures, described below, were used to evaluate initial status only, and still others to evaluate final status only.

1. Measures Used to Evaluate Initial Status and Change: (*a*) The Discomfort Scale* consists of a total of 41 items, each of which is rated by the patient on a four-point scale. The items are concerned with psychic or somatic complaints which the patient may have experienced and are rated in terms of the relative distress or lack of it they have caused the patient for the week preceding his filling out of the scale. Each item is scored on the four-point scale as follows: severe distress, 3; moderate distress, 2; slight distress, 1; no complaint, 0, so that a higher total score indicates greater discomfort. This scale was filled out by the patient in the presence of a member of the research staff initially and at the time of reevaluation.

(*b*) The Ineffectiveness Scale* measures the degree of ineffectiveness in a patient's interpersonal relationships with people who are significant in his day-to-day living. There are 15 categories of behavior included in the scale.† The ratings are based on both the degree of ineffectiveness (or inappropriateness) of the behavior in question and the frequency with which it occurs in major life settings. For each patient, ratings are based on the combined judgments of an interviewer of the patient and a concealed observer of the interview, and a similar pair of raters of an interview with a relative. The scale is filled out initially and at the time of reevaluation.

2. Measures Used to Evaluate Initial Status Only: (*a*) The Prognostic Inventory* consists of 72 items thought to have prognostic relevance to the patient's acceptance of and response to psychotherapy. The items are scored "yes" or "no" and are grouped as follows: (1) orientation to therapy; (2) history of illness, including onset, course, and effects of previous treatment, if any; (3) early family relationships; (4) early response to family stress; (5) social relations with same and opposite sex; (6) school history, including maximum grade attainment, reason for leaving, extracurricular activities; (7) group experience in organized groups since leaving school; (8) leisure-time activities; (9) employment record, including performance, reason for changes, aspirations, job movement, level of responsibility, and additional or part-time jobs; (10) emotional responsibility,

* The data in the present report are based only on those measures marked with an asterisk.

† The categories are overly-independent, superficially sociable, extrapunitive, officious, impulsive, hyperreactive, overly systematic, overly dependent, withdrawn, intrapunitive, irresponsible, overcautious, constrained, unsystematic, and sexual adjustment.

and (11) financial responsibility. These items are scored by the psychiatrist and social worker based on information received by them in their respective interviews with patient and relative.

(*b*) The Sway Test* presumably is a measure of suggestibility.[23] The test procedure consists of blindfolding the patient and silently observing him for two minutes, then suggesting repetitively in a monotone that he (the patient) is falling forward. The measure is the change in sway produced by the instructions. The results were dichotomized in terms of "sway" or "no sway."

(*c*) The Porteus Test is a standard series of mazes of increasing difficulty and was administered in the routine manner.[24] The qualitative error score suggested by Porteus was employed as a possible measure of planfulness.

(*d*) The Psychotherapy Motivation Checklist was developed by the research staff shortly after the first reevaluation of treated and drop-out patients and has been applied retrospectively to all patients in the project. It comprises a series of items which systematically assess those factors which motivate patients to continue in or leave treatment. The checklist includes such items as the patient's and his relatives' attitude toward psychotherapy, severity of presenting complaints, motivation of referring source, degree of success in previous treatment, possible conflict of treatment with patient's religion, threat of treatment to patient's employment, and family status.

3. Scales or Instruments Used to Evaluate "Change" Only: (*a*) The Inventory of Extra-Therapeutic Factors was devised to evaluate those variables outside of formal treatment which potentially contribute to a change in the patient's status. It takes into account possible modifications in the patient's life situation, such as the loss of a job, an increase in salary, death in the family, divorce from spouse, new religious affiliation, medical treatment, etc.

(*b*) Therapists' ratings of their own patients were done by the three resident psychiatrists independently each time the patients were evaluated by the research staff. The therapists were asked to rate the patients' status on a four-point scale of improvement and to comment on observed changes in behavior either in or outside treatment.

## Results

In collecting data for this exploratory study, we pursued leads that occurred to us or were suggested in the literature. The data are presented in terms of the instruments used to collect them.

*A. General Data.*—Of the 91 patients included in the research study, 28, or 31%, left treatment prior to the fourth treatment session. This figure is smaller than most of the attrition rates of psychiatric outpatients reported in the literature, which range from 30% to 65%. One reason for this may be that patients with antisocial character disorders and alcoholics, who are the ones most likely to terminate treatment prematurely, were not included in the study. Another may be that patients and therapists were urged to remain in contact for at least six months. Patients who left treatment did not differ significantly from those who remained in age, sex, or marital status. As reported elsewhere,[25] our results confirmed those of other investigators that there is a class difference with respect to remaining in psychotherapy. Social-class ratings on our final sample showed that of 54 lower-class patients, 22, or 41%, dropped out before the fourth session, while of 28 middle-class patients, only 6, or 21% did the same. Thus the drop-out rate for lower-class patients is about double that for middle-class ones. Because of its apparent importance, the class factor will be considered again in conjunction with some of the findings to be presented.

*B. Aspects of Patients' Illness.*—Patients diagnosed as having anxiety reactions or depressive reactions remained in treatment significantly more frequently than all the others.‡

Clinical review of the data suggests a relationship between prematurely leaving treatment and duration of illness before seeking treatment, and whether the illness had been fluctuating or stationary. If patients were divided on the basis of clinical history into those who had suffered from the present illness 10 or more years and those who had been ill 2 years or less, it was found that the latter group tended to drop out of treatment significantly more frequently than the former.§ An interpretation of this finding is offered below.

On a clinical basis, we found that patients with fluctuating illnesses were significantly

‡ $\chi^2=3.89$ $P<0.05$.
§ $\chi^2=6.64$ $P<0.01$.

more likely to remain in treatment than those whose condition had been relatively stationary.‖ Prognostic scale items dealing with this showed a similar trend (Table).

*C. Scores on Initial Measures.*—Comparison of drop-outs and remainers with respect to their scores on initial measures revealed the following:

1. Suggestibility (sway test): Since acceptance of psychotherapy may be a function of the patient's need and desire for advice or the extent to which he is accessible to authority influence, a measure of suggestibility, sway, was examined for its relationship to attendance in treatment. It was found that patients who sway tend to remain in treatment, while those who do not sway tend to drop out.¶ If only patients assigned to group and individual psychotherapy were considered, the relationship was found to be stronger.[26] It appears, then, that the factor of suggestibility has important implications for the drop-out problem.

2. Initial Scores on Discomfort Scale: For the total population, drop-outs and remainers did not differ on the initial discomfort scores, nor did lower- and middle-class patients. It was noted, however, that lower-class patients who dropped out of treatment had significantly lower initial average discomfort scores than did lower-class patients who remained. The mean initial discomfort score for the former group was 33.3; for the latter, 42.4.# Middle-class patients who dropped out did not show this tendency; that is, their initial discomfort scores did not differ from the scores of middle-class patients who stayed, and both were about the same as the scores of lower-class patients who remained in treatment. One possible explanation for this finding, like the one on duration of illness, is that lower-class patients who are reluctant to accept psychotherapy convey this by consciously or unconsciously minimizing their complaints, which in their eyes are the only reasons for being given treatment. Since there were only six middle-class patients who dropped out, as compared with 22 lower-class ones, conclusions about them are hazardous, but it can be said that these 6, at least, did not show this tendency.

3. Initial Scores on Ineffectiveness Scale: Over-all, there were no significant differences between patients who remained and those who left treatment, or between lower- and middle-class ones. In contrast to their initial discomfort scores, lower-class patients who left treatment scored as high on the Ineffectiveness Scale as those who remained, so that the relative lack of reported discomfort in those who dropped out cannot be explained on the basis that they were less "sick," at least in terms of social ineffectiveness.

One item on the Ineffectiveness Scale, that concerned with sexual functioning, did distinguish significantly between those who remained in treatment and those who left.* The latter tended to deny any difficulties in this area, while the former tended to reveal sexual problems of varying degrees of severity. Among other possibilities, this finding could be interpreted on the same basis as the reported greater duration of illness and greater discomfort in the treated group. That is, it might simply reflect the fact that patients who remain in psychotherapy are more apt to confide their difficulties honestly to the interviewer. The others are apt to be more guarded, or to resent what they regard as unwarranted prying into this aspect of their affairs.

4. Prognostic Inventory: Inspection of the Prognostic Inventory suggested certain trends which, though for the most part not statistically significant, seem worth reporting and discussing in an exploratory study such as this, especially since they formed a meaningful pattern, consistent with other findings of this investigation and the results reported by others. The accompanying Table lists those items of the Prognostic Inventory which were scored relatively more frequently by remainers or drop-outs respectively.

‖ $\chi^2=10.97$ $P<0.02$.

¶ $\chi^2=3.43$ $P<0.10, >0.05$.

\# $t=1.94$ $P<0.10, >0.05$.

* $\chi^2=6.18$ $P<0.02$.

*Prognostic Inventory Items Related to Remaining In and Dropping Out of Treatment*

| | Items Related to | | | |
|---|---|---|---|---|
| | Item No. | Remaining | Item No. | Dropping Out |
| I Orientation to therapy | 1 | Sees treatment as means of self-modification | 3 | Comes to treatment under compulsion |
| | 2 | Sees treatment as means of vindication | | |
| II History of illness and previous treatment | 10 | Fluctuating past year | 11 | Stationary past year |
| | 12 | More than 6 mo. previous psychotherapy | | |
| | 13 | Above, with benefit | | |
| III Early family stress and response to it | | | 16 | Continuous parental conflict |
| | | | 22 | Dealt with family stress actively |
| IV Schooling | 36 | Graduated from high school or better | 38 | Failed to complete elementary school |
| V Group relations | 44 | Member 2 or more organized post-school groups | 34 | Has formed only superficial relationships with others |
| | 51 | Participant in individual competitive sports | 46 | Member of no organized post-school groups |
| VI Employment | 55 | Housewives | 64 | Missed promotions colleagues received |
| | 66 | Managerial or professional work | | |
| | 67 | Customary additional jobs | | |

It will be seen from the Table that, with respect to orientation to therapy, patients who see therapy as a means of modifying themselves (Item No. 1) or who remain in therapy to vindicate themselves (No. 2) tend to remain, while patients who come to treatment under compulsion (No. 3) tend to drop out. With respect to their illness, patients with fluctuating illness (No. 10) tend to remain; those with stationary illnesses (No. 11), to drop out. Those who have had at least six months of previous psychotherapy (No. 12) and who benefited from it (No. 13) might be expected to accept this form of treatment again, and so they do.

Since the therapist in many ways may represent a parental figure, we wondered whether previous experience with parents would influence a patient's attitudes to psychotherapy and included some items to test this. It appeared that patients whose parents were in continuous, direct conflict (No. 16) tended to drop out of treatment. Perhaps their life experience did not imbue them with much trust in parents or their substitutes. Patients who as children dealt with family stress actively by, for example, trying to outwit their parents or defend one against the other also tended to leave treatment early (No. 22), perhaps as an expression of counterdependency.

With respect to schooling, in confirmation of findings of others, we found that less than grammar-school education predisposed to dropping out (No. 38). Contrariwise, high-school graduates tended to remain in treatment (No. 36).

Since psychotherapy cannot proceed unless patient and therapist can establish a meaningful relationship, we thought that patients' capacity to establish such relationships, as demonstrated in their social life, might be relevant to their acceptance of therapy. There is some evidence from the Prognostic Inventory that this might indeed be the case. Thus, patients who had established only superficial relationships with others (No. 34) or who belonged to no organized groups (No. 46) tended to leave therapy. Patients who had participated in groups (No. 44) or in individual competitive sports, such as golf, track, or chess (No. 51), tended to remain in treatment. Participation in groups and games also suggests a certain reliability and goal-directedness which we believe is relevant to acceptance of psychotherapy.

Finally, with respect to employment, we found that housewives (No. 55) tended to stay in treatment, largely a reflection, we believe, of the fact that it was relatively easy for them to get to the clinic during working hours. Patients with managerial, professional jobs (No. 66) or who had additional part-time jobs (No. 67), indicating goal-directedness and perseverance, tended to stay in treatment; those who failed of promotions their colleagues received, perhaps indicating a lack of these traits, did not (No. 64).

Certain items cast a little light on the personal attributes associated with class mem-

bership which are related to staying in or leaving treatment. Consistent with the finding that lower-class patients do not remain in psychotherapy as long as middle-class ones, most of the items related to staying in treatment were scored more frequently by middle-class patients; most of those related to dropping out were scored oftener by lower-class patients. Of the 11 "remainer" items, all but No. 10 (fluctuating illness) were scored proportionately more frequently by middle-class than by lower-class patients.

Of the eight items related to leaving treatment, four were scored proportionately oftener by lower-class patients, and only one oftener by middle-class patients. Lower-class patients scored predominantly on No. 3 (comes to treatment under compulsion), No. 11 (illness stationary during past year), No. 38 (did not complete elementary school), and No. 46 (belongs to no organized groups). Middle-class patients scored predominantly on No. 64 (missed promotion his contemporaries have had), probably because fewer lower-class patients have jobs which are within a hierarchy.

These findings suggest that among the attributes related to class position which influence remaining in treatment are attitude to psychotherapy (1, 2, 12, 13 *vs.* 3), educational level (36 *vs.* 38), and group participation (44, 51 *vs.* 46).

*D. The Therapy Situation.*—1. Patients' Reasons for Seeking Treatment: A study of reasons expressed by patients for seeking treatment [27] indicated that for about two-thirds of them the act of accepting or refusing psychotherapy changed the balance of forces in their relationships with persons important to them. For these patients, remaining in therapy seemed partly determined by whether this affected the balance of forces favorably or adversely.

A further finding was that the reasons patients gave for remaining in treatment bore no relation to how long they remained. That is, patients who gave "appropriate" reasons for entering psychotherapy, such as desire to modify themselves, were no more likely to stay than those who gave "situational" reasons, such as to please a spouse or get a husband to stop drinking. We believe that this finding is to be understood in the light of the fact that for many patients psychotherapy carries a stigma. Some of those who genuinely want it are therefore unable to admit this, but find it less damaging to their self-respect to attribute their presence in the psychiatric clinic to external pressures. The reasons a patient gives for seeking psychotherapy are determined not only by his actual condition but by other motives, such as protection of his self-esteem. They must be interpreted as representing, at least in part, patients' efforts to adapt to the stress of the psychotherapy situation.[28]

An additional possibility is that some patients who are genuinely inadequately motivated at first are converted to a more positive view of psychotherapy by the psychiatrist in the initial therapeutic interview.

2. Type of Psychotherapy: The influence of type of therapy on the drop-out rate is affected by many factors, including patients' expectancies, attributes of the treatment situation itself, and aspects of the psychiatrist's attitudes. The drop-out rate varied considerably among the patients assigned to the three types of treatment (whether they came to the first therapy session or not), being 44% for those assigned to group therapy, 27% for minimal contact therapy, and 14% for individual therapy. If only patients who came to at least one session are considered, the difference in drop-out rate in the three types of treatment, although it is still in the same direction, diminishes appreciably. This suggests that patients' anticipation of treatment, even before they actually experience it, affects their willingness to come to the first meeting. Group therapy is the most at variance with patients' expectations of psychotherapy.

In this connection it is worthy of comment that more patients failed to show up for the first group session than for the other two forms of treatment, even though patients had to agree in advance to take whatever treat-

ment was offered them in order to be accepted in the project. Apparently some patients agreed to this who had no intention of coming to group treatment, in the hope of being assigned to individual therapy.

After patients come to treatment, there is some evidence that group therapy is the most stressful in that, in contrast to the other two forms, which showed no such trend, patients who dropped out of group therapy were more socially ineffective than those who remained.[26] However, as indicated in the next section, once a patient is familiar with his psychiatrist, the relationship between them seems to be a more potent factor than the type of treatment in determining whether or not he remains.

3. Psychiatrist: Analysis of the drop-out rate from the standpoint of the three psychiatrists involved in the experiment highlights the desirability of including a study of the influence of the therapist's attitudes on whether patients accept treatment. Psychiatrist A, for example, had a drop-out rate of only 8%, as compared with 33% and 26% for the other two psychiatrists. Moreover, of the 11 patients who came to group therapy at least once but left before the fourth session, only one was from the group of Psychiatrist A.

In this connection the previous group therapy experience of these psychiatrists is relevant. Psychiatrist A had no losses from a group which he organized from the waiting list. Psychiatrists B and C each inherited leadership of a group they had observed and added new patients of their own choice to it. None of the patients, including the new ones, dropped out of these groups.

In this research, it will be remembered, the psychiatrist had no choice as to who entered his group and did not know the patients previously. This may have affected the attitudes of the three psychiatrists differentially, influencing, in turn, their drop-out rates.

E. Remaining in Psychotherapy and Improvement: In discussing suitability for psychotherapy, aspects of patients related to their remaining in treatment are seldom distinguished from attributes related to likelihood of benefit from treatment in patients who stay. The results of this study suggest that at times this distinction may be useful. Using a significant decrease in social ineffectiveness after six months as a criterion of improvement, it was found that certain factors related to remaining in or leaving treatment were also related to improvement, certain were unrelated, and some were negatively related. For example, although fewer lower- than middle-class patients stayed in treatment, those who did improved as much as the middle-class ones. Patients who had, according to their reports, been sick a long time were more likely to stay in treatment than those who reported a shorter duration, but those who were ill a shorter time improved more. A history of fluctuating illness was associated both with staying in treatment and improvement in treated patients, as were the diagnoses of anxiety and depression.

Suggestibility, as determined by the sway test, was found to be positively related to remaining in treatment but unrelated to improvement.[25]

With respect to the Prognostic Inventory, patients who sought therapy as a means of modifying themselves or to vindicate themselves tended to stay in treatment. The former attitude was unrelated to improvement; the latter, negatively related to it. Educational level was positively associated with remaining in treatment but was unrelated to improvement. Housewives, who could come to treatment easily, tended to remain in therapy, but this item was unrelated to improvement. Items related to participation in groups tended to be related to both remaining and improving.

With respect to the therapeutic situation, the psychiatrist seemed to affect both remaining in treatment and improvement, in that the same psychiatrist who had the fewest drop-outs tended to have the highest improvement rate in those who remained. With regard to the type of therapy, patients

who remained in group therapy improved at least as much as those receiving the other two forms, although the drop-out rate from group therapy was greater than from the other two.[21]

Pending the obtaining of follow-up data on improvement, these results must remain highly tentative and do not warrant full discussion. They suggest, however, that the ability to establish relationships with others, whether from the side of the psychiatrist or the patient, is positively related to both staying in psychotherapy and benefit from it. Other attributes of patients, such as suggestibility, education, and class position, may be related only to remaining in treatment. Remaining in treatment, though a necessary condition for improvement, is obviously not a sufficient one.

## Comment

The results obtained in this study tend, on the whole, to confirm clinical impressions as to attributes of patients related to their suitability for treatment stated in books on psychotherapy, and are also consistent with the quantitative studies of Veterans Administration Mental Hygiene Clinics. The time, therefore, seems ripe for an attempt to generalize concerning some of the factors related to remaining in or leaving treatment by psychiatric outpatients.

Our population differs somewhat from that on which books on psychotherapy are based, on the one hand, and from the Veterans Clinic population, on the other. Writers on psychotherapy have, as indicated above, made the observations on a preselected group of patients, more uniform as to class position and education than the clinic populations. Hence it is not surprising that none of the four books reviewed,[7,9,11] makes mention of socioeconomic determinants of suitability for treatment, for example. Our population differs from that of the VA clinics in two chief respects. It contains a preponderance of women; theirs is almost exclusively male. Because of the design of the research, our population contains no patients who would be classed as "psychopathic," other than the very few who slipped through the diagnostic screen. Since many veterans who fall within this diagnostic spectrum are not eligible for outpatient treatment at a VA clinic, they are probably not heavily represented in the above-mentioned studies either, but the percentage would be greater. As a result of these differences, conclusions drawn from the three populations—private patients, clinic patients, and veterans—tend to supplement each other; but no serious contradictions emerge.

The findings of the studies mentioned above, including the present one, can be grouped under nine interrelated categories. Since these studies stress characteristics of the patient, six of the categories refer to personal attributes, and three, on which there are fewer data, to aspects of the therapy situation. The six categories of personal attributes are as follows: social, economic, and educational status; verbal intelligence; readiness to communicate distress and weakness; influenceability; social integration, and perseverance. The three pertaining to therapy are relation of therapy to the patient's life situation, characteristics of the therapist, and characteristics of the therapy situation. Since these categories are overlapping, many items can be classified under several headings. To avoid reduplication, items have been placed under those headings to which they seem most appropriate. Data bearing on each category will now be reviewed.

*A. Personal Attributes of Patients.*—1. Social, Economic, and Educational Status: These factors are grouped because they are not independent. Their implication for remaining in therapy is indirect. That is, a person's occupation and education, which are related to his social status, imply certain things about his intelligence, readiness to communicate distress, perseverance, and so on, factors which are more directly related to his attitude toward psychotherapy. It has been well established that the lower a patient's class, the less apt he is to remain in

psychotherapy.[25,29] This is implied also in a combined vocabulary, occupation, and education index used by Rubinstein and Lorr, which was found to be significantly higher with the remainers than the terminators.[12] Those studies which considered occupation and education separately found the same relationship to exist. Hiler [13] noted a higher educational level in those who remained in treatment. We found that patients who had completed high school tended to remain; those who failed to complete elementary school tended to drop out.

2. Nature of Illness: The only consistent finding in the literature with respect to diagnosis is that patients with anxiety reactions tend to stay in treatment. We found this tendency, as did Hiler and Wolberg.[11] One might expect that patients who express their difficulties in terms of somatic symptoms would be less suitable candidates for treatment than those who freely admit emotional or interpersonal difficulties, and many writers report this. Hiler found that patients who dropped out had more somatic symptoms, a finding also reported by Dengrove and Kutash.[14] Pumpian-Mindlin [10] believes that patients who talk chiefly of interpersonal problems are better candidates for treatment than those who stress symptoms. One of us, however, in another study found no relationship between whether patients in group therapy stressed somatic or emotional complaints and their acceptance of treatment.[30] Pumpian-Mindlin says that whether or not a patient stays does not depend on the seeming severity of the illness, and Cameron [7] says that "no adequate selection can be made . . . upon diagnosis alone."

We suspect that the basic problem here lies in the vagueness of the relationship between diagnostic categories or psychiatric symptoms and patients' habitual ways of relating to others. The same psychiatric symptoms can appear in a wide variety of interpersonal contexts, and different ones can express the same interpersonal difficulties. Moreover, since psychotherapy is a new interpersonal situation for patients, their complaints may change as a result of the developing contact with the therapist. For example, presenting somatic complaints may be an indirect way of expressing reluctance or inability to reveal personal problems, which sometimes is overcome after therapy starts.

With respect to duration of illness, we found unexpectedly that patients who stated they had been ill a long time remained in treatment more frequently than those who indicated a shorter duration of illness. We are inclined to regard this as a manifestation of willingness to communicate, discussed below.

The finding that patients with fluctuating illnesses are more apt to remain than those with stationary ones may have several implications. Fluctuations in a patient's condition suggest that pathogenic and restorative forces are still in active conflict without having reached a stable equilibrium. This would heighten the patient's awareness that he is ill and so increase his motivation to seek help. Moreover, fluctuations in severity often occur in response to changes in the patient's life situation, thus indicating that he is accessible to interpersonal influences, a point considered more fully below. For this reason, he might be accessible to the beneficial interpersonal influence represented by psychotherapy, and therefore remain in it.

3. Readiness to Communicate Distress and Personal Liabilities: The more skilled a person is in the use of language, the greater the likelihood that the task of psychotherapy would make sense to him; so it is not surprising that those investigators who measured verbal intelligence found it to correlate with remaining in therapy. Vocabulary is part of the combined measure used by Rubinstein and Lorr which was related to remaining in treatment. Hiler found that the acceptors of treatment gave more responses on the Rorschach test and had a higher verbal-conceptual intelligence on the Wechsler-Bellevue scale. Auld and Eron [18] confirm this finding and look upon the verbal-intelligence factor as the chief

determinant both of the Rorschach finding and of acceptance of treatment. It may be related to the greater psychological sophistication reported by Hiler, and what Colby [8] calls the ability to express oneself and grasp the other's verbal communications.

With respect to the degree of distress the patient reveals, there is general agreement that the worse a patient says he feels, the more likely he is to accept treatment. The degree of the patient's expressed distress is an indicator both of the strength of his motivation for treatment and of his willingness to communicate with the therapist. Rubinstein and Lorr noted that remainers were rated as "sicker" and indicated that they felt worse than rejecters. Dollard and Miller [29] believe that the more miserable a patient is the greater his motivation to try to learn patterns of response which could diminish his distress; hence the better his prognosis. We found degree of expressed distress to be related to remaining in or leaving of treatment in lower-class patients only, those who dropped out scoring considerably lower on the discomfort scale than those who stayed. Apparently their degree of complaining was in part an indirect expression of their attitude toward psychotherapy.

Reported duration of illness, which we found to be positively related to remaining in treatment, may be similarly viewed as more relevant to the patient's willingness to communicate than to the actual length of time he had been ill. The interviewer's estimate as to how long a patient had been ill before seeking treatment depended primarily on the patient's report and that of a relative, supplemented in some cases by previous clinical records. Patients who remain in treatment are more likely, we believe, to maximize the severity and duration of their illnesses as justification for seeking treatment than those who reject treatment. The latter are more likely to minimize their condition or, if they speak of previous illness, to describe it in different terms from the current complaint.

The courage to reveal unflattering aspects of oneself is another facet of willingness to communicate. Colby regards this as a favorable prognostic sign. Hiler found that remainers were more willing to reveal confidential material and inner feelings, expressed more inferiority feelings, and were less evasive than rejecters. Rubinstein and Lorr found that remainers expressed more dissatisfaction with themselves. Our results are equivocal on this point. Patients who were scored on the Prognostic Inventory as seeing psychotherapy as a means of self-modification, implying that they were dissatisfied with themselves, tended to stay in treatment. But whether those who stayed in initially gave situational or appropriate reasons for seeking treatment was not related to how long they stayed. This indicates again that experience with psychotherapy may overcome an initial communication block. In this connection we found that patients who had had at least six months of previous psychotherapy stayed in it again.† It is possible that our finding, also mentioned by Wolberg, that patients whose parents were in conflict tended to drop out may also be relevant here, since such a family atmosphere could well lead to a child's unwillingness to expose his own feelings.

4. Influenceability: The process of psychotherapy involves influence on one person by another. The influence may be exerted with varying degrees of subtlety. At one extreme, it may consist of facilitating the patient's emotional growth in accordance with his own potentialities; at the other, it may involve direct suggestion. Hence accessibility to influence might be expected to be related to remaining in therapy. This could operate at the very beginning, in that the patient has to accept the psychiatrist's word for it that psychotherapy will help him. The patient's remaining thereafter continues to depend to some extent on his willingness to

† The clinicians regard previous psychotherapy, if unsuccessful, as a poor prognostic sign (Ingham and Love,[9] Wolberg [11]), but this may be true only with respect to likelihood of improvement, not acceptance.

accept the therapist's influence. Hence personal factors, such as suggestibility, rigidity, and attitudes to authority figures, would be expected to be related to remaining in therapy. We found a positive relationship between primary suggestibility, as measured by a sway test, and remaining in treatment.[25] Since we are inclined to regard a fluctuating illness as evidence of responsiveness to interpersonal influences, the tendency of these patients to remain in treatment may also be subsumed here.

Dengrove and Kutash suggest that the clinic should base its acceptance of patients for treatment on their amenability to influences. They found that patients who dropped out were more apt to be antagonistic to doctors and Veterans Administration personnel. Rubinstein and Lorr noted that terminators were more aggressive, apt to act out their feelings, and hostile to authority. Hiler found them to be more paranoid. Our finding that patients who reacted actively to family stress tended to leave treatment may be relevant here.

Finally, both Rubinstein and Lorr and Hiler found the remainers to be more flexible and less rigid or stereotyped in their thinking than the terminators.

5. Social Integration: Persons who are accustomed to interacting with others in a constructive way would be apt to perceive psychotherapy as potentially rewarding and also to participate in this type of social relationship. Wolberg speaks in this connection of patients who have achieved social maturity, can gratify vital needs in conformity with the group. Ingham and Love[9] stress "relatability"—the ease with which a patient can allow himself to develop rapport. Rubinstein and Lorr found terminators to be characterized by nomadism and high scores on a "psychopath" scale, and Hiler found more character disorders in this group. Our population excluded these persons by design, but we also found that patients who participated in group activities tended to remain in treatment, whereas isolated ones, or those who had only superficial relations with others, tended to leave.

6. Perseverance: The habit of seeing things through despite obstacles would be expected to be revelant to remaining in psychotherapy, which is a long-term task, requiring considerable tolerance for frustration, and there is a good deal of indirect evidence that this is so. This attribute is implicit in many of the factors that have been mentioned above, such as occupational and educational level and nomadism. Among the clinicians, Wolberg and Ingham and Love stress ability to tolerate stress without repressive or regressive reactions or disruption of the personality. Related to this, Wolberg and Pumpian-Mindlin refer to the degree of accord between a patient's ambition and achievement. Presumably, the lower the discrepancy, the more persevering the patient. Particularly pertinent is the finding of Rubinstein and Lorr that more remainers than terminators completed a given level of education, regardless of the actual educational level achieved; that is, they completed the task they had undertaken. They also found more job changes among the terminators and more restlessness. Hiler found more status striving, drive, and ambition among the remainers and less unemployment. We found more failure to achieve normal promotion among those who left treatment. Regular participation in sports, which implies perseverance, seemed to be positively related to staying in treatment.

It perhaps should be made explicit that readiness to communicate, influenceability, social integration, and perseverance are closely related. Nomadism, for example, may be an expression of fear of being influenced by others, and long-term participation with others implies some ability to persevere. Both social integration and influenceability imply some skill in communicating feelings and understanding communications about them from others. Much further study would be required to determine exactly how the group of variables included in these broad categories are related to each other.

*B. Aspects of the Treatment Situation.*—1. Relation of Treatment to the Patient's Life Situation: Although only one of the studies reviewed here [14] was primarily concerned with situational factors relating to acceptance or rejection of treatment, the little information that is available about them is again highly consistent. These factors may be grouped as motivational or mechanical factors. The motivational factors have to do with the effect of treatment on the patient's relationships with other important persons; the mechanical ones, on the presence or absence of obstacles to treatment. These are interdependent. The stronger the drive, the greater the obstacle required to prevent the patient from remaining in treatment. Also, patients notoriously use mechanical reasons as excuses for dropping out, when actually they do not wish to continue. Nevertheless, for present purposes, motivational and mechanical factors may be conveniently considered separately.

(*a*) Motivational Factors. Whether or not a patient remains in treatment may depend on how it influences the balance of forces in his power struggles with persons important to him. In such cases, he will stay in treatment as long as it strengthens his hand. Thus, Dengrove and Kutash note that some patients remained in treatment only as long as they thought this would enable them to receive a pension, and that patients who came in direct response to outside pressure were apt not to stay. Koren and Goetzel [17] reported the same, as do Cameron and Ingham and Love. In such cases acceptance of therapy would represent a defeat for the patient. As noted above, we found no such relationship between apparent presence or absence of outside pressure as reported by the patients and remaining in treatment. We did find that patients who came to vindicate themselves tended to stay.

Two difficulties in evaluating motivational factors may again be mentioned. One is that the reasons a patient gives for seeking treatment may not correspond with the actual ones, especially if admission of need for treatment is felt by the patient as a threat to his self-respect. That is, a patient's communications at the start of treatment may primarily represent his way of attempting to adapt to the situation, rather than a truthful expression of his actual inner state. The other is that the patient's attitude may change as the result of his initial exposure to the treatment situation.

(*b*) Mechanical Factors. We found that housewives, who had no difficulty attending during the hours that the clinic was open, and often welcomed this chance to get out of the house, tended to remain in treatment more frequently than students or persons regularly employed. For the latter, attending weekly involved inconvenience and sometimes jeopardizing of job or loss of income. Koren and Goetzel note that having to come a long distance and conflict with job were determinants of leaving treatment. Rickler et al.[19] found that 12 of 40 private patients who did not return after the first visit said that they could not afford it or that it interfered with their jobs. Wolberg mentions that treatment must not impose too great a hardship on the patient.

2. Personality of the Therapist: The therapist's capacity to inspire trust in his patients will obviously influence whether they return to him. We found that one of the three participating psychiatrists had a definitely lower drop-out rate than the other two. Since our study was not focused on this problem, we did not explore the reasons for this difference. Hiler, however, notes that warm, friendly, competent therapists kept more patients in treatment than those rated as least warm and friendly. Dengrove and Kutash mention such factors as a therapist's ill-concealed hostility to alcoholics or an overbearing manner as related to patients leaving treatment. Koren and Goetzel stress the therapist's difficulty in establishing a satisfactory relationship with the patient as a cause of their terminating treatment.

3. Aspects of Treatment: Obviously, aspects of the treatment itself will determine its attractiveness to patients. Dengrove and

Kutash list many features of management which influence whether or not a patient keeps coming back. These include the therapist's missing appointments, the patient's having to pass through too many hands before getting into treatment, short duration of interviews, and too much sharing of information about patients, so that they lose faith in the confidentiality of treatment. We found that individual treatment had a higher stay rate than either minimal therapy or group therapy. This was most marked if patients who did not come to the first meeting were included in the calculation, suggesting that anticipation of the treatment situation may play an important role. Group therapy and minimal contact treatment sounded less attractive than individual treatment. Considering only patients who attended one meeting, the difference in favor of individual therapy was less. This suggests that the patient-therapist relationship could overcome initial unfavorable anticipations.

Of these nine categories, perseverance can best be regarded as a character trait which is relatively independent of the particular task the person has undertaken. Its importance for prognosticating whether or not a patient will remain in psychotherapy lies in the fact that this is a long-term task, often involving considerable frustration, and without a clearly defined goal. The other eight can all be regarded as influencing or expressing the patient's motivation for or against staying in psychotherapy. As such, they are dependent on the interplay between personal attributes and the particular qualities of the psychotherapeutic situation. This interaction determines the balance between the patient's need for therapy and the obstacles to obtaining it, which is largely determined, in turn, by his perception of psychotherapy. Those attributes of psychotherapy which we believe to be most relevant here are a continual interaction with a prestige figure who offers help, in which the task is to express one's feelings and problems. The goal is increased self-knowledge as the means to improved comfort and social effectiveness.

Class, education, and verbal intelligence all are related to the patient's acceptance or rejection of increased self-knowledge as a sensible and helpful goal.[29,31] A life pattern of long-term social interaction with others might also be expected to predispose a patient favorably to the therapy situation. Thus, isolates, nomads, and those who establish only superficial relationships with others tend to leave psychotherapy, while socially integrated persons tend to remain in it. Since a common feature of all psychotherapies is that the therapist is a prestigeful person who tries to influence the patient by his personality or technique, accessibility to such influence would be expected to be related to the patient's perception of therapy as potentially helpful. Patients who demonstrated this accessibility by swaying to suggestion tend to stay in treatment; opinionated, rigid, paranoid patients, and those who may have learned through bad experiences with parents to distrust authority figures, do not. Since the benefits of psychotherapy are obtained through talking about oneself, readiness to communicate would be expected to be related to staying in treatment. This readiness or the lack of it is implied in most of the categories just mentioned. It also shows itself in the nature and kind of distress the patient reveals. Patients who freely express distress (especially in the form of anxiety) and dissatisfaction and who present psychic problems tend to remain in psychotherapy. Those who are evasive, indicating distrust of the situation, or stress somatic ills, suggesting that they seek a different type of treatment, tend on the whole to drop out.

In this connection, many of the findings reported in this paper converge on the point that patients' initial communications must be considered in part as their efforts to adapt to the therapy situation. Thus, some of our patients said they would accept group therapy if assigned to it when they had no intention of doing so, in order to be accepted in the treatment program and so have a chance of obtaining individual treatment. Whether patients gave appropriate or situ-

ational reasons for coming to treatment was unrelated to whether they stayed in treatment or improved, suggesting that both types of reasons might be partly attempts to deal with stresses of coming to psychotherapy, and did not correspond to their actual motivations. Unwillingness of drop-outs to reveal sexual difficulties and their tendency to report somatic rather than psychic complaints may be understood in the same way, as can the tendency of lower-class patients who left treatment to report less discomfort than those who stayed. Finally, the fact that remainers reported they had been ill longer than drop-outs suggests that they were more eager to impress the psychiatrist with their need for help.

From the standpoint of the treatment situation, the patient's perception of it as useful or not depends in part on its place in his current life situation. If submitting to it represents a yielding to outside pressures, and so weakens his power position, he tends to reject it. Mechanical obstacles, such as interference with job, may have a similar effect. Finally, the personal qualities of the therapist and the nature of the specific treatment situation may influence the patient's julgment as to whether he will find the help he expects, and so partly determine whether or not he remains in treatment. The patient's experience in the initial interviews, however, may be sufficient to counteract his initial unfavorable or defensive attitudes toward therapy, so that there are many exceptions to the generalizations offered above.

Preliminary results suggest that attributes of patient, therapy, and therapist related to the patient's remaining in treatment need not be related to whether those who do remain improve under it. Follow-up studies of the patients in this project are expected to yield data bearing on this problem.

## Summary

Study of 91 psychiatric outpatients, in conjunction with a review of relevant literature, leads to the following tentative generalizations with respect to factors determining whether or not a patient will stay in psychotherapy.

Attributes of the patient which are positively related to remaining in treatment are class, education and occupation, fluctuating illness with manifest anxiety, readiness to communicate distress and personal liabilities, influenceability, social integrity, and perseverance. With respect to the treatment situation, its relation to the patient's life situation, aspects of the treatment itself, and attributes of the therapist influence whether or not a patient will stay. Some of the factors which determine whether a patient will remain in treatment may differ from those determining improvement in patients who do remain.

Department of Psychiatry, The Johns Hopkins University School of Medicine.

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# Verbal Behavior Analysis

*Some Content and Form Variables in Speech Relevant to Personality Adjustment*

**LOUIS A. GOTTSCHALK, M.D.; GOLDINE C. GLESER, Ph.D., Cincinnati, and GOVE HAMBIDGE Jr., M.D., Minneapolis**

One of the commonest forms of behavior that typifies man is verbal behavior. While to a great extent man's pattern of speech is determined by the grammar and rhetoric of the language he speaks, it is reasonable to assume that within this framework the individual's choice of words, themes, and style of speech may reveal something of his personality dynamics and his current emotional state. Indeed, psychiatrists make this assumption daily in their interpretation of what the patient is saying in therapeutic sessions, but the cues he uses are for the most part subjective and unsystematized.

Many investigators have engaged in studies of verbal behavior using various stimuli to produce verbal activity, such as the clinical interview, the interpretation of proverbs, and Thematic Apperception Test cards. Also, various methods of categorizing the obtained materials have been utilized. No attempt will be made to review their work here, but interested readers may consult the reviews by Mowrer,[8] Pronko,[9] and Sanford.[10] It may be noted, however, that the method of eliciting speech affects the results obtained,[4] so that comparison of results of various investigators is often difficult. In our own work we have felt that it was essential to maintain a standardized method for eliciting verbal samples when comparing different samples.

In our program of research on verbal behavior we have made preliminary steps along three main avenues of approach which we believe may be fruitful in determining the relationship of speech patterns to personality variables. These are (*a*) the determination of the effect of specific stimuli, such as pharmacologic agents, biologic deprivation (e. g., of food), or anxiety-producing situations, on the individual speech pattern[5]; (*b*) the study of the relationship between language patterns and psychodynamic patterns as they emerge in patients undergoing psychoanalytic treatment,[4,6] and (*c*) the investigation of the differences in form and content variables among groups of persons differing in psychiatric diagnosis or in personality adjustment.

The present report is of the last type and aims to describe some comparative studies of short samples (five minutes) of speech, elicited in the same standardized way and produced by two major groups of persons: a group of hospitalized psychiatric patients, and a matched "control" group of nonhospitalized subjects who had no disabling personality disorder. The purposes of this study were twofold. It was, in part, an attempt to search for and to test content and form variables in speech that may be particularly relevant to personality adjustment, and it was a preliminary study of the differential language patterns occurring in patients with neurotic and psychotic types of personality disorders.

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## Method

The subjects used in this study were 11 patients hospitalized for psychiatric illness and 11 volunteers who were gainfully employed and were functioning adequately. Some attempt was made to match the two groups with regard to age, sex, and educational background. The biographical data are presented in Table 1.

TABLE 1.—*Biographical Data on Subjects*

| | | Nonhospitalized, Socially Adjusted Volunteers | Psychiatric Inpatients |
|---|---|---|---|
| Age | Mean | 33.8 | 26.4 |
| | Range, yr. | 25-48 | 18-47 |
| Sex | Male | 8 | 8 |
| | Female | 3 | 3 |
| Race | Negro | 2 | 4 |
| | White | 9 | 7 |
| Education | College | 4 | 1 |
| | Junior college | 4 | 5 |
| | High school | 2 | 1 |
| | Grade school | 1 | |

It may be noted that the main difference between the groups in these factors is a significant difference ($P<0.05$) in mean age. However, it is doubtful whether this small difference in average age, within the range covered by these subjects, is relevant to variations in patterns of speech. We intend to check this point in future studies.

Habits of speech were elicited from these subjects by "verbal" and "visual" methods of induction, previously described elsewhere.[4] The "verbal" method simulates the psychiatric interview situation and elicits speaking by use of the following standard instructions: "This is a study of speaking and conversational habits. Upon a signal from me, I would like you to start telling me about any interesting or dramatic life experiences you have had. Once you have started, I shall be here listening to you, but would prefer not to reply to any questions you may feel like asking me until the five minutes are up. Do you have any questions you would like to ask me now before we start? Well, then, you may start." The "visual" method simulates the projective test situation and elicits talking by asking the subject to tell stories suggested by four Thematic Apperception Test cards, in order of presentation, 7GF, 13MF, 2BM, and 3BM.

## Results

Content elements in the verbal samples were analyzed according to categories previously established and described[4] and listed in Table 2 of this article. Since comparison of the data obtained under the two methods of elicitation had revealed considerable differences in the patterns of language produced, it was decided to study primarily the data obtained by verbal induction.

The mean, median, and range of each of the content variables obtained under verbal elicitation are presented in Table 2 for the two groups of subjects. It should be noted that all variables are expressed as the percentage of words falling in that category relative to the total number of words in the sample. The two groups of subjects were compared on each of the variables listed in Table 2, using the Mann-Whitney test for determining the significance of the difference in the distribution of values or, roughly speaking, in the medians. Table 2 also presents the critical ratio for each variable and the significance levels for those variables for which the difference approaches significance.

The groups were founded to differ significantly at the 1% level on one of the 28 verbal categories tested. That is, the group of psychiatric inpatients had a larger mean percentage of verbs of all types in the five-minute sample. Four additional variables differed significantly at the 5% level. The group of psychiatric patients used a smaller proportion of words indicating a sense of belonging to a group (specifically, such words as "we," "us," "our," etc.), more references to the self, fewer references to

TABLE 2.—*Significance of Differences in Percentages of Various Content Categories Occurring in Language Samples Elicited by "Verbal" Induction from a "Normal" and a Psychiatric Inpatient Group*

| Category | Symbol | "Normal" Group | | | Psychiatric Inpatient Group | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Median | Mean | Range | Median | Mean | Range | T* | P |
| Total material objects | O | 16.6 | 16.3 | 11.2-21.0 | 16.7 | 17.7 | 13.1-25.5 | 0.623 | |
| Self | S | 4.6 | 5.3 | 0.1-10.5 | 9.9 | 9.1 | 2.5-12.9 | 2.230 | 0.05 |
| Self-other | SO | 1.4 | 1.7 | 0- 3.9 | 0 | 00.9 | 0- 4.9 | 2.040 | 0.05 |
| Others | o | 4.6 | 4.8 | 2.6- 9.8 | 5.0 | 4.7 | 0.5- 9.3 | 0.295 | |
| Things | T | 3.9 | 4.1 | 0- 7.1 | 1.6 | 1.9 | 0- 9.3 | 2.298 | 0.05 |
| Total abstractions, concepts | C | 12.8 | 13.1 | 9.2-17.5 | 14.4 | 14.4 | 8.9-24.5 | 0.590 | |
| Measure (space, time, quantity) | c | 6.2 | 6.6 | 3.9-11.6 | 7.3 | 6.5 | 3.5- 9.9 | 0.010 | |
| Action | CA | 4.1 | 4.6 | 2.5- 8.8 | 5.5 | 6.7 | 2.1-17.0 | 1.083 | |
| State or quality | C8+CQ | 1.8 | 1.8 | 0.7- 3.2 | 1.4 | 1.2 | 0- 3.1 | 1.608 | |
| Total verbs | V | 20.8 | 20.5 | 16.5-25.8 | 24.0 | 24.2 | 20.1-27.4 | 2.659 | 0.01 |
| Perception | P | 0.5 | 0.5 | 0- 1.8 | 0.2 | 0.3 | 0- 1.0 | 1.411 | |
| Rumination | R | 1.1 | 1.5 | 0.2- 3.6 | 1.6 | 2.1 | 0.4- 5.7 | 1.215 | |
| Incipient action | IA | 0.4 | 0.7 | 0.1- 2.3 | 1.5 | 1.7 | 0- 4.2 | 1.674 | 0.10 |
| Neuromuscular action | A | 8.8 | 8.9 | 7.7-11.3 | 10.2 | 10.1 | 6.3-12.8 | 1.573 | |
| Auxiliary verbs | VD | 9.1 | 8.9 | 7.0-12.0 | 9.8 | 10.1 | 8.2-14.1 | 1.674 | 0.10 |
| Total references to measure (space, time, quantity) | M | 20.8 | 21.6 | 17.8-29.9 | 19.1 | 19.3 | 9.3-30.2 | 1.149 | |
| Quantity | q | 5.2 | 5.7 | 1.3- 9.0 | 6.3 | 6.3 | 3.5-10.2 | 0.590 | |
| Time | t | 5.4 | 5.2 | 3.0- 7.7 | 5.4 | 5.0 | 0.7- 8.2 | 0.361 | |
| Spatial relation | s | 9.7 | 10.7 | 6.6-16.3 | 7.0 | 8.2 | 4.1-14.1 | 1.871 | 0.06 |
| Total qualifying words | Tq | 42.9 | 41.0 | 35.2-46.2 | 34.0 | 35.8 | 29.9-45.2 | 2.166 | 0.05 |
| Adjectives | AD | 11.2 | 11.2 | 7.5-14.8 | 10.5 | 9.7 | 4.8-14.2 | 1.600 | |
| Prepositions & articles | xD | 23.5 | 22.3 | 11.4-27.2 | 18.2 | 19.2 | 14.7-27.0 | 1.838 | 0.07 |
| Adverbs | yD | 7.1 | 7.5 | 4.7-10.9 | 7.0 | 6.8 | 4.5- 9.2 | 0.689 | |
| Conjunctions | zD | 8.4 | 8.6 | 6.7-11.0 | 7.7 | 7.9 | 4.1-10.9 | 0.624 | |
| Negations | n | 1.3 | 1.4 | 0.5- 2.9 | 2.0 | 2.2 | 1.0- 5.8 | 1.936 | 0.06 |
| Interjections | I | 0.3 | 0.3 | 0- 0.7 | 0.2 | 0.5 | 0- 1.7 | 0.361 | |
| Words implying definiteness | Da | 24.2 | 24.5 | 21.2-29.4 | 25.7 | 26.2 | 21.1-29.1 | 1.710 | 0.08 |
| Words implying indefiniteness | Di | 4.5 | 4.7 | 3.3- 6.9 | 4.1 | 3.9 | 2.6- 6.9 | 1.411 | |

* By Mann-Whitney test.

inanimate objects (things), and fewer qualifiers (adverbs, adjectives, prepositions, and articles) than did the control group. Two other variables, spatial references (regardless of part of speech) and words of negation, differed at the 6% level of significance. Other trends of possible interest were that concepts of state or quality and prepositions and articles appeared relatively less frequently in the group of psychiatric inpatients, whereas verbs of action (e. g., run, talk) and incipient action (e. g., love, wish) were relatively high for the group of psychiatric inpatients, as were also words of all sorts conveying definiteness or accuracy.

Previous work of ours[4] had indicated that the ratios verbs of action plus objects divided by verbs of action plus objects plus concepts (A+O/A+O+C), and verbs of action divided by verbs of action plus adjectives (A/A+adjectives) might be related to different types of adjustment to inner conflict. The former ratio was found in one patient to be related to a desire to take in food or to be loved and the arousal of internalized restrictions against the expression or acting out of such impulses, whereas the latter was related to a more diffuse drive to action and associated internalized restrictions. The latter ratio is similar to the verb-over-adjective ratio, noted by other investigators[1,2] as tending to be related to anxiety. On the basis of our findings in these two groups of subjects, two other ratios were investigated, i. e., total verbs divided by total verbs plus total qualifying words (V/V+Tq) and references to self divided by reference to all persons, including self (S/SO+S+O).

The mean, median, range, critical ratio, and level of significance of these ratios are shown in Table 3. For the first two ratios, a one-tailed test of significance was used,

TABLE 3.—*Significance in Differences in Patterns (Ratios) of Content Categories Occurring in Language Samples Elicited by "Verbal" Induction from a "Normal" and a Psychiatric Inpatient Group*

| Ratio | "Normal" Group | | | Psychiatric Inpatient Group | | | T* | P |
|---|---|---|---|---|---|---|---|---|
| | Median | Mean | Range | Median | Mean | Range | | |
| $\frac{A+O}{A+O+C}$ | 0.68 | 0.668 | 0.54-0.74 | 0.67 | 0.659 | 0.50-0.78 | 0.13 | |
| $\frac{A}{A+AD}$ | 0.44 | 0.446 | 0.36-0.55 | 0.51 | 0.515 | 0.38-0.72 | 1.54 | 0.06 |
| $\frac{V}{V+Tq}$ | 0.33 | 0.335 | 0.27-0.42 | 0.43 | 0.406 | 0.33-0.48 | 2.53 | 0.01 |
| $\frac{S}{SO+S+O}$ | 0.37 | 0.415 | 0.01-0.75 | 0.57 | 0.617 | 0.40-0.96 | 1.97 | 0.05 |

* By Mann-Whitney test.

since these were based on the a priori hypothesis that these ratios would be higher in the group of psychiatric inpatients.

The ratio A+O/A+O+C did not differentiate the two groups. The second ratio, (A/A+adjectives), was higher for the hospitalized psychiatric patients, with a difference that was significant at the 6% level. The trend here was consistent with the hypothesis, but the difference did not quite reach a convincing level of significance. The similar ratio, (V/V+Tq), however, was highly significant under a two-tailed hypothesis; thus it appears substantiated that a higher verb-adjective or similar ratio is characteristic of some kinds of maladjustment, although more research is necessary to determine the best way to measure this aspect of verbal behavior and also to delineate more exactly the nature of the personality differences to which it is related.

Actually, with regard to distinguishing the two samples reported here, the percentage of verbs alone yields as good a differentiation as the ratio verbs over verbs plus qualifying words. The productions of 9 of the control subjects contained less than 22.5% verbs, whereas this was true for only 3 of the 11 psychiatric patients. The percentage of qualifying words is highly correlated (negatively) with the percentage of verbs and hence adds nothing to the prediction.

The final ratio, (S/SO+S+O), is significantly higher for the psychiatric inpatient group but, again, is no more predictive than is S alone.

While the two groups represented in this sample are quite distinct, the difference between them is a complex of many possible factors, any one or all of which could be related to the differences in verbal behavior found. Thus, differences in verbal behavior might relate to degree of mental adjustment, hospitalization as compared with nonhospitalization, the high proportion of psychotic schizophrenics or of other psychotics in the sample of psychiatric patients, and so forth. A tentative study of these possibilities could be explored by subdividing the two groups on the basis of a rating of over-all social adjustment and looking for trends in the variables found to differentiate the two groups as a whole. Five of the nonhospitalized, socially adjusted group were rated as better adjusted and six as somewhat less well adjusted. Six of the psychiatric inpatient group were rated as showing neurotic and five as showing psychotic adjustment.* It was reasoned that if the average score on a variable showed a continuous trend from

* The diagnoses for the neurotic group were as follows: emotionally unstable personality, 3; neurotic-depressive reactions, 1; anxiety reaction, 1, and schizoid personality, 1. The diagnoses for the psychotic group were as follows: schizophrenic reaction, paranoid type, 2; schizophrenic reaction, simple type, 1; schizophrenic reaction, chronic undifferentiated type, 1; involutional psychotic reaction, 1.

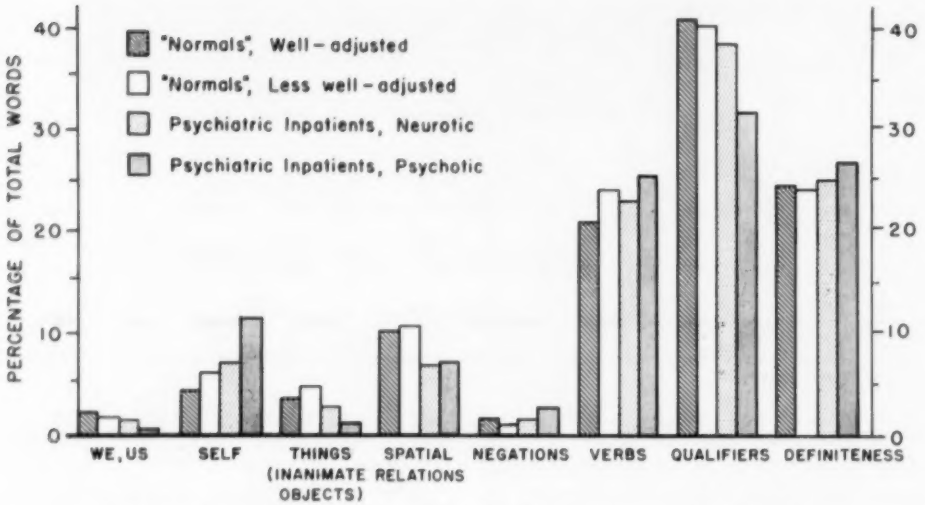


Fig. 1.—Trends in mean percentage scores of selected word categories for four groups differentiated on the basis of over-all adjustment.

best to least adjusted (psychotic), the variable involved was suggestively related to level of adjustment. But if the differences were such that the two nonhospitalized subgroups were alike and the two psychiatric inpatient groups alike, the variable might be related to (1) level of adjustment (the presence of an interpersonal malfunctioning disabling enough to require hospitalization) and/or (2) the effect of hospitalization itself. Also, where the psychotic group differed widely from the other three, the difference might be mainly related to the psychotic versus the nonpsychotic type of adjustment.

The mean values in the four subgroups on those variables approaching significance in the over-all analysis are shown in Figures 1 and 2. There is a clear downward trend from best- to least-adjusted groups for the variables: percentage of references to identification with the group, "we," "us," and so forth (SO), and percentage of qualifying words (Tq). There is a definite upward

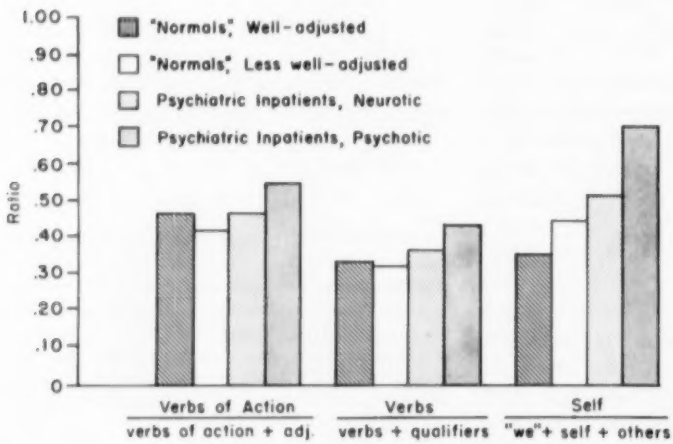


Fig. 2. — Trends in mean ratios among certain word categories for four groups of subjects differentiated on the basis of over-all adjustment.

trend for percentage of self-references (S) and for the ratio S over SO+S+O. However, for both self-references and qualifiers the psychotic group differs significantly from each of the three other groups ($P<0.05$). For percentage of verbs and words implying definiteness, the two "control" groups (well adjusted and less well adjusted) are about equal, but there is an upward trend from them through the definitely neurotic group to the psychotic group, so that these variables also appear to relate to adjustment level, although possibly at a grosser level. The greater use of negation, on the other hand, seems to be more closely related to psychotic processes, since the difference between the "control" and psychiatric inpatient groups seems to lie mainly in the psychotic group. The differences among the groups on the variable of percentage of spatial references (s) is rather interesting. Here the two "control" groups are about alike and the two psychiatric inpatient groups are alike, though the "control" and the psychiatric inpatient groups differ significantly. It might be suspected, therefore, that this variable is related to confinement and might be found lowered in other hospitalized or confined groups.

It was thought that it might be of interest to investigate whether the differences found between the "control" and the psychiatric inpatient group in verbally induced verbal samples were also present in the visually induced samples. It should be noted that the absence of such differentiation would in no way invalidate the results obtained, since the verbal productions obtained in response to the request to tell a story about a picture were known to be quite different from those obtained when the person was requested to relate a life incident (previous report [4]). The visually induced talking tended to be more constrained in many respects and resulted in a slower rate of speech, a smaller incidence of self-references, verbs of action, concepts, and "measures" (words indicating a relationship in time, space, or quantity regardless of grammatical usage), and a greater incidence of references to material objects and the use of auxiliary verbs than did the verbally induced talking. However, it was felt that if differences in verbal patterns were found which transcended the means of initiating the speaking, the importance of the different verbal patterns would be enhanced.

Table 4 presents the means, medians, and ranges of the word variables used by the two groups in their "visually" induced verbal samples for those variables which were found to approach significance in the "verbally" induced samples. Significance levels are given on the basis of the one-tailed hy-

TABLE 4.—*Significance of Differences in Percentages of Various Content Categories Occurring in Verbal Samples Elicited by "Visual" Induction from a "Normal" and a Psychiatric Inpatient Group*

| Category | Symbol | "Normal" Group | | | Psychiatric Inpatient Group | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Median | Mean | Range | Median | Mean | Range | $T$* | $P$ |
| Total objects | O | 17.7 | 18.3 | 11.9-28.9 | 21.8 | 22.0 | 18.5-26.9 | 2.561 | 0.01† |
| Self | S | 3.2 | 3.1 | 0.6- 6.7 | 2.5 | 3.5 | 0.3- 9.3 | 0.263 | -- |
| Things | T | 4.8 | 4.3 | 1.3- 6.8 | 4.3 | 5.0 | 2.7- 8.4 | 0.558 | -- |
| Total concepts | C | 10.6 | 10.8 | 5.4-18.4 | 10.6 | 10.2 | 4.7-15.2 | 0.263 | -- |
| Total verbs | V | 21.1 | 22.7 | 17.3-30.6 | 25.9 | 25.0 | 20.5-29.8 | 1.445 | 0.08 |
| Incipient action | IA | 1.1 | 1.0 | 0- 1.9 | 0.5 | 0.9 | 0- 3.0 | 1.214 | Difference reversed |
| Neuromuscular action | A | 6.5 | 6.3 | 3.8- 7.9 | 7.0 | 7.0 | 4.3- 9.1 | 1.510 | 0.07 |
| Auxiliary verbs | VD | 12.2 | 11.7 | 7.8-15.2 | 12.8 | 12.7 | 9.6-15.4 | 0.952 | -- |
| Spatial relations | s | 6.8 | 6.4 | 3.3-10.9 | 7.9 | 7.9 | 3.3-13.4 | 1.379 | Difference reversed |
| Total qualifying words | Tq | 42.6 | 40.2 | 30.3-50.9 | 36.7 | 36.3 | 29.2-42.7 | 1.870 | 0.03 |
| Negations | n | 1.3 | 1.5 | 0.2- 3.7 | 2.1 | 2.0 | 0.5- 4.4 | 1.083 | 0.14 |

* By Mann-Whitney test.
† Two-tailed test.

pothesis. It may be noted that the psychiatric inpatient group again used relatively more verbs, more negatives, and fewer qualifying words (Tq) than did the "control" group, the last-mentioned difference reaching statistical significance. No difference between the groups was noted for the use of self-references and words implying definiteness. A slight reverse trend was noted in the relative use of word symbols for inanimate objects (T) and spatial relationships (s).

### Form Analysis

Certain aspects of the form of verbal behavior were analyzed statistically. These included number of words less number of fills (uh's, ah's, and er's), repetitions of words or phrases, and number of fills, incomplete words, nonverbal expressives (coughs, laughs, etc.) and aposiopeseis. The mean, median, and range of each of these variables for the two groups are shown in Table 5, together with critical ratios obtained by the Mann-Whitney test.

TABLE 5.—*Significance of Differences in Percentages of Various Form Variables Occurring in Language Samples Elicited by "Verbal" Induction from a "Normal" and a Psychiatric Inpatient Group*

| Category* | "Normal" Group | | | Psychiatric Inpatient Group | | | | |
|---|---|---|---|---|---|---|---|---|
| | Median | Mean | Range | Median | Mean | Range | T† | P |
| F | 21 | 28.3 | 2-65 | 11.5 | 15.0 | 0-43 | 1.543 | 0.12 |
| R | 4 | 5.9 | 0-17 | 4 | 4.4 | 0-10 | 0.131 | ... |
| INC | 1 | 1.1 | 0-3 | 0 | 0.7 | 0-3 | 0.853 | ... |
| NVE | 1 | 1.3 | 0-5 | 1 | 1.2 | 0-4 | 0.033 | ... |
| APO | 2 | 2.5 | 0-10 | 1 | 1.6 | 0-5 | 0.590 | ... |
| W-F | 613 | 617.2 | 456-803 | 526 | 496.3 | 147-815 | 1.740 | 0.08 |

* F=fills (uh's, ah's, and er's); R, repetitions of words or phrases; INC, incomplete words; NVE, nonverbal expressives (coughs, laughs, etc.); APO, aposiopeseis; W-F, words minus fills.
† By Mann-Whitney test.

The only variable which approaches significance in this analysis is the number of words used per five minutes ($P=0.08$). This variable was investigated further in terms of the trend in rate of speech from minute to minute in both the verbally and the visually induced samples. In both cases the two groups started at about the same rate, but the psychiatric inpatient group appeared to exhibit a downward trend in rate of speech, while the "control" group remained relatively constant. The significance of these trends was investigated for each group separately by analysis of variance and the results are shown in Table 6. In both the verbally induced and the visually induced samples the downward trend for the psychiatric inpatient group is significant ($P<0.01$; $P<0.05$), while there is no significant trend for the "control" group. In the verbally induced samples there is also a significant difference between the groups in over-all rate of speech ($P=0.05$) and in the group-time interaction ($P=0.01$). The group-time interaction is a measure of the difference in trend, and the fact that it is significant implies that there is a real difference in the trends for the two groups under verbal induction. The psychiatric inpatient group was characterized by a decrement in verbal production from beginning to end, particularly marked in the last two minutes, while the "control" group spoke at an approximately constant rate throughout the five-minute interval. A further examination of the data revealed no difference in trend in rate of speech between the two "normal" groups divided on the basis of adjustment. The neurotic group showed some diminution in rate of speech in the last minute, but the over-all downward trend was primarily due to the psychotic group, who had low rates of speech for the second, fourth, and fifth minutes. Furthermore, these low rates were a result of long pauses (15 seconds or longer) rather than a persistent and continuous slowing of speech.

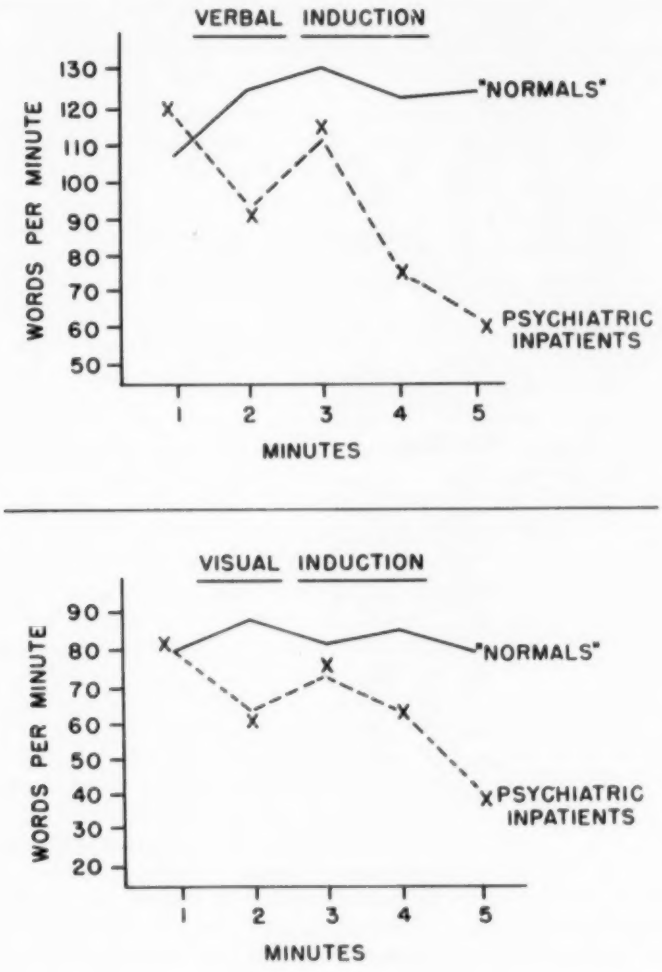


Fig. 3.—Comparison of rate of speech of "normal" and psychiatric inpatient groups under verbal and visual induction.

## Comment

The working assumption of this study is that habits of speech reflect a person's characteristic orientation toward the self, external objects, and reality. In this study we have tried to learn whether small groups of subjects with different degrees of psychosocial maladjustment reflect their personality problems in their habits and patterns of speech.

There are obviously serious methodologic problems in such an investigation, one of which is the selection of language variables that have more relevance to personality than to the structure of language and rhetorical conventions. This preliminary study has helped single out some language variables that appear to be promising insofar as they reflect a person's orientation to himself, external objects, and reality. Another problem is that of determining optimum and yet standardized sampling conditions for comparative evaluation.

We have found that a single subject giving multiple verbal samples shows a fairly wide range of ways of expressing himself in terms of the verbal categories we have analyzed.[4,6] The frequency of use by one sub-

TABLE 6.—*Analysis of Variance of Rate of Speech of "Normal" and Psychiatric Inpatient Groups*

| Source of Variance | DF | Sum of Squares | Mean Square | *F* | *P* |
|---|---|---|---|---|---|
| **Verbal Induction** | | | | | |
| "Normals" | | | | | |
| Subjects | 10 | 20,846.13 | 2,084.61 | | |
| Time | 4 | 3,729.80 | 932.45 | 1.94 | n.s. |
| Error | 40 | 19,177.60 | 479.44 | | |
| Total | 54 | 43,753.53 | | | |
| Inpatients | | | | | |
| Subjects | 10 | 90,286.84 | 9,028.68 | | |
| Time | 4 | 23,727.77 | 5,931.69 | 4.35 | 0.01 |
| Error | 40 | 54,570.83 | 1,364.27 | | |
| Total | 54 | 168,584.44 | | | |
| Over-all | | | | | |
| Subjects | 20 | 111,132.97 | 5,556.65 | | |
| Group | 1 | 25,050.90 | 25,050.90 | 4.51 | 0.05 |
| Time | 4 | 10,328.42 | 2,582.10 | 2.80 | 0.05 |
| Group×time | 4 | 17,127.16 | 4,281.79 | 4.64 | 0.01 |
| Error | 80 | 73,749.43 | 921.87 | | |
| Total | 109 | 237,388.87 | | | |
| **Visual Induction** | | | | | |
| "Normals" | | | | | |
| Subjects | 10 | 21,639.04 | 2,163.90 | | |
| Time | 4 | 1,149.80 | 287.45 | | n.s. |
| Error | 40 | 15,481.60 | 387.04 | | |
| Total | 54 | 38,270.44 | | | |
| Inpatients | | | | | |
| Subjects | 10 | 26,059.71 | 2,605.97 | | |
| Time | 4 | 9,222.26 | 2,305.56 | 2.53 | 0.05 |
| Error | 40 | 36,503.74 | 912.59 | | |
| Total | 54 | 71,785.71 | | | |
| Over-all | | | | | |
| Subjects | 20 | 47,698.75 | 2,384.94 | | |
| Group | 1 | 8,784.44 | 8,784.44 | 3.68 | n.s. |
| Time | 4 | 6,774.90 | 1,693.72 | 2.61 | 0.05 |
| Group×time | 4 | 3,597.16 | 899.29 | 1.38 | n.s. |
| Error | 80 | 51,985.34 | 649.82 | | |
| Total | 109 | 118,840.59 | | | |

ject of any single category appears to depend on a complex of variables: the methods by and situations in which the speech is elicited, the past history of the subject, and the present psychodynamic state of the subject.[4-6] It is likely that a person shows notable differences in language patterns within his own particular range of variation in a monologue as contrasted with a dialogue, in written as contrasted with spoken language, when fasting as compared with nonfasting, and so forth. There are no studies that have specifically demonstrated such, but our previous investigation leads us to expect these effects, and we are in the process of studying these matters now. Until it is shown that such situations do not appreciably affect the language patterns of a subject, we think it is necessary to standardize rigorously the experimental conditions under which verbal samples are obtained for investigations of comparative language patterns of people who fall into different psychiatric nosologic classifications.

Other investigators have explored spoken language patterns in neurotics and psychotics as compared with those of a "normal" group of persons. Lorenz and Cobb[7] have reported interesting differences in the verbal behavior of neurotics and psychotics. The verbal material of these authors, however, was not elicited from the psychotic group in quite the same way that it was from the other groups. Also, the types of verbal categories analyzed were not always comparable to those analyzed in the present study. They found more frequent use of the pronoun "I" by their "neurotic" than by either their psychotic or their "control" group. Their psychotic group was composed of paranoid

schizophrenics, and "I" was used with about the same frequency as it was used by the "normal" group.

The differences in speech patterns we found in our psychotic group as compared with the better-adjusted groups do not coincide well with the differences reported by Lorenz and Cobb. We are inclined to attribute these discrepancies to two possible factors: 1. The authors did not standardize the method of eliciting speech in their groups of subjects. 2. The psychotic group we studied contained only two paranoid reaction types, whereas in the Lorenz-Cobb study the psychotic group was composed completely of paranoid schizophrenics. We have already discussed the importance of the first factor. Insofar as the second factor is concerned, we are obliged to conclude, tentatively, that speech patterns, like other clinical manifestations of people with this condition, may indicate the paranoid schizophrenic to be less deviant from the well-functioning person than other schizophrenic reaction types, except for the paranoid schizophrenic's seriously overemphasizing *others* as initiators of activity involving the self instead of properly considering the role and impulses of the self in evaluating the nature of his interpersonal relations. Lorenz and Cobb have found a relative verbal preoccupation in the paranoid schizophrenic with others, particularly with the word "he," and this is a finding that one might predict from clinical observation. We believe the study of the verbal behavior of paranoid schizophrenics is important and should be repeated under more carefully controlled conditions. Our present study cannot clarify the problem any further.

Fairbanks,[3] comparing the verbal responses in interpreting and elaborating on proverbs of a group of schizophrenics and "normals," found more use of negations and self-references and fewer references to words indicating group affiliation ("we," "our," "us") in the schizophrenics than in the nonschizophrenics. Our findings tend to corroborate those of Fairbanks, even though her method of eliciting verbal activity was dissimilar to ours.

At this stage of our investigations into verbal behavior, we should prefer not to discuss in detail any implications of our findings of some differences in the speech patterns of the well adjusted and the maladjusted. Our tentative impression is that the findings are consistent with the concept that mental illness is a complex reaction involving disorganization of social relationships and that the nature and severity of the social malfunctioning are reflected in the kinds of symbols of verbal expression and communication that are used. Considerably more research is needed before we can relate specific patterns of speech to any particular type of personality configuration. For this reason, we are planning and carrying out studies on a larger series of subjects, using the most promising verbal categories found in this study, as well as exploring the relevance of some others.

## Summary

An attempt has been made to search for and to test content and form variables in speech that are relevant to personality adjustment and to explore in a preliminary way whether there are different language patterns in neurotic and in psychotic reaction types.

Eleven psychiatric inpatients and eleven subjects not hospitalized for a psychiatric illness were given instructions to talk, without interruption, for five minutes in response to two methods of eliciting speech, one of which simulated the clinical psychiatric interview ("verbal" induction) and the other of which simulated the projective test situation ("visual" induction).

Out of 28 "content" categories studied, 5 were found to differ significantly ($P<0.01$-$P<0.05$) in frequency of use by these two groups of subjects when the speech was elicited by the "verbal" method of induction. The five categories were (1) words indicating a sense of belonging to a group (first person plural pronouns, such

as "we" and "us"), less frequent in the psychiatric inpatients; (2) words referring to the self, more frequent in the psychiatric inpatients; (3) words indicating processes (verbs), more frequent in the psychiatric inpatients; (4) words referring to inanimate objects, less frequent in the psychiatric inpatients, and (5) words that qualify other words, less frequent in the psychiatric inpatients. Two categories were found different in frequency of use at the 6% level of significance: (1) words indicating location or spatial relationship (regardless of grammatical use), less frequent in the psychiatric inpatients, and (2) words indicating negation, more frequent in the psychiatric inpatients. The frequency of occurrence of four more categories of words tended to differentiate the two groups and may be worth studying further, although the differences found did not reach a convincing level of significance: (1) concepts (abstractions) referring to a state or quality; (2) words referring to processes, verbs of action (e. g., "run," "talk"); (3) verbs of incipient action, i. e., those indicating a feeling or emotion (e. g., "love," "wish"), and (4) words indicating definiteness or accuracy (regardless of grammatical use).

When the speech was elicited by the "visual" method of induction, the group of psychiatric inpatients again used relatively more verbs, more negations, and fewer words that qualify other words, but only the last difference reached statistical significance. In other respects, too, the verbal data produced under the conditions of the "visual" method of induction were dissimilar in pattern to those obtained with the "verbal" method of induction.

Certain ratios of word categories were analyzed and found to differ significantly in their use by the two groups, but the ratios did not appear to be of any more predictive value than one or more of the single-word categories of which the ratios were composed.

Certain aspects of the form of verbal behavior were analyzed, and only one of these approached significance ($P=0.08$), that is, the average number of words spoken in five minutes by the two groups. The group of psychiatric inpatients did show, however, a significant downward trend in rate of speech per minute both in the verbally induced ($P<0.01$) and in the visually induced ($P<0.05$) samples of speech. The nonhospitalized subjects showed no significant trend in variations in rate of speech per minute for either type of five-minute verbal sample.

Further analysis of the differences in the language patterns of the group of psychiatric inpatients and the group of relatively well-adjusted nonhospitalized subjects, when each group was divided into better- and poorer-adjusted subgroups, suggested that some of these differences were related stepwise to the level of personality (social) adjustment, from well adjusted to less well adjusted to neurotic and to psychotic.

The hospitalized patients as a group, however, uttered significantly fewer words referring to location or spatial relations than the nonhospitalized subjects, and no stepwise differences were noted relevant to the subgroups. So this variable may possibly be determined more by confinement than by type of adjustment pattern.

The implications of these preliminary findings are briefly discussed.

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# Adjustment Patterns of Leadership and Defenses in a Disturbed Child Group

IRVING M. GOLDSTEIN, Ph.D.; ILSE JUDAS, M.D.; HELEN A. SUTTON, R.N., and EUGENE I. FALSTEIN, M.D., Chicago

When a child enters a clinic, hospital, or institution for treatment, it is usual to think that it is *his* problem to adapt to an environment that by sheer numbers, tradition, and authority sets the rules and limits of behavior and therapy. Despite the convenience of this assumption, our experiences and anxieties often indicate that it is the staff, patients, even the building and the grounds that must bend toward the newness, unpredictability, and lack of knowledge suddenly confronting the child. Whether the interactive result is integrative or disruptive, our anticipations (rarely disappointed) are toward the change of a new configuration. On the children's psychiatric unit at the Institute for Psychosomatic and Psychiatric Research and Training of the Michael Reese Medical Center we found over a period of time that the parsimonious but practical criteria of admission acceptance, such as age, size, pubescence, type and degree of psychiatric dysfunction, and degree of psychological and developmental regression, often yielded individual and group frustrations that we could ill predict. Our theories, diagnoses, treatment goals, therapeutic endeavors, and planning were for an individual, but the bulk of the living experiences was within assigned and circumscribed groups. Once the new child was placed in a group, the mold and partners of his activities were set—eating, gym, bike riding, school, etc. On a closed residential unit such as this one, children's groups are more likely to be artificial than spontaneous. Almost arbitrarily, roommates, table seating, and routines of bathing, dressing, occupational therapy, and outdoor walks are assigned rather than chosen.

During the history of the unit, three groups have evolved. On admission, the new patient, if he was a boy, over 7 years old, in reasonable command of toilet habits, able to talk and attend school, and exhibiting some potential for interaction, was placed in the "boys' group." An aggregation of autistic, mute, and organically injured children under 7 years of age composed the second group. In addition, there was a "girls' group." It was customary for the head nurse and psychiatrist to form a quick decision about placement at the time of admission, based on scant knowledge of the new child's history and his behavior during admission procedures. The uncertainty of the criteria for group placement and the obvious disruption within the group and total unit when a new member was introduced, encouraged the need for a study that could delineate more scientific criteria for the psychological processing of admissions and groupings, rather than the capricious, if educated, hunches we employed.

The backdrop for the study was the breakfast grouping. Out of the many activities available, it was chosen because of its convenience, its suitability for recording,

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Formerly at Institute for Psychosomatic and Psychiatric Training and Research, Michael Reese Medical Center; now at Veterans Administration Hospital, Sepulveda, Calif. (Dr. Goldstein). Clinic Physician (Dr. Judas), Head Nurse, Child Care Unit (Miss Sutton), Attending Psychiatrist and Chief of Child Care (Dr. Falstein), Institute for Psychosomatic and Psychiatric Research and Training, Michael Reese Hospital.

the universal meaningfulness of the eating situation, and the catalytic effect on spontaneous verbalizations. The boys' group had permanent seating arrangements around the table. The girls sat close by and offered opportunity for extragroup interaction. Their overt and individual value patterns concerning food could be observed easily through excessive demands, rejection, messing, and food fantasies. Generalized feelings about the nurses who fed them came quickly to the surface. A potpourri of oral, anal, genital, hostile, and passive themes was readily evidenced at mealtime. These often were aimed at the two nurses who sat with the group. The role of the *group nurse* was defined in terms of her usual everyday functions. She served food, participated in conversations, defined reality in disputes, and provided restrictive control when necessary. The *observer-nurse's* role was more artificial, as a passive but participating observer. She encouraged topics that pointed toward fantasies and then withdrew. The other team members, a psychologist and a psychiatrist, observed the total interactions through a one-way mirror and tape-recorded the proceedings. The last three team members rated the types of interactions immediately after each session, and pooled ratings were used for all final descriptions of group process. Twenty-four half-hour breakfast sessions, spaced at intervals of one or two a week over a four-month period, were recorded. A sequence of 17 sessions relatively free of technical and procedural difficulties will be presented here.

The object of our study was the boys' group, since it was fairly well integrated, needed less individual supervision and guidance, and historically had the highest percentage of successsfully treated cases. These boys had accepted an adult leadership which centered in a succession of male aides who conducted sports activities. Their own leadership had been relatively firm over a long period of time, but at the beginning of the study they faced the future prospect of losing their leader, who was known to be close to hospital discharge. Their integration was also potentially more dangerous because of concerted action in revolts, attacks on younger children, and destruction of property.

For the evaluation of the group process, the two areas of group leadership and individual defense patterns were selected. In a general way, these areas could encompass the relative stability of the group process and, at the same time, measure the sequential individual forces which were effective or ineffective in producing changes.

## Methodology

*A. Data Collection.*—Four steps and techniques were employed for the collection of immediate ratings.

1. Tape Recording: Each session was divided into three 10-minute intervals. A hidden microphone installation allowed tape recordings to include all group participants. The psychologist and psychiatrist observed each session through a one-way mirror while monitoring the tape recording.

2. Sequence-Rating Schema: At the end of each 10-minute interval, the observers completed a Sequential-Rating sheet which described one or more major interactions (Figure 1 is an example of the initial interval in Session XII). The observer-nurse rated the interactions after the end of each complete half-hour session.

3. Qualitative Description: At the end of each session, each observer wrote a short behavioral description of the over-all interactions, emphasizing leadership roles.

4. Adjective Check List: A standardized check list of behavioral variables (e. g., defiant, agitated, imaginative, etc.) was utilized in the early sessions to amplify descriptions, but it was found to duplicate the qualitative reports and therefore was abandoned.

*B. Summary Ratings.*—After all data were collected for the 24 sessions, pooled ratings were obtained in the following manner:

The tape recording for each session was replayed while each observer reviewed his Qualitative Description and Sequence-Rating Schema. A pooled description of the themes, leadership modes, and individual roles was then agreed upon. Four classes of variables were chosen to indicate the direction and preferred modes of reaction: Intellectual, Motoric, Interpersonal, and Personal. In turn, these variables were respectively subdivided into complementary categories: Intellectual: (1) Fantasy, (2) Reality; Motoric: (1) Acting-Out

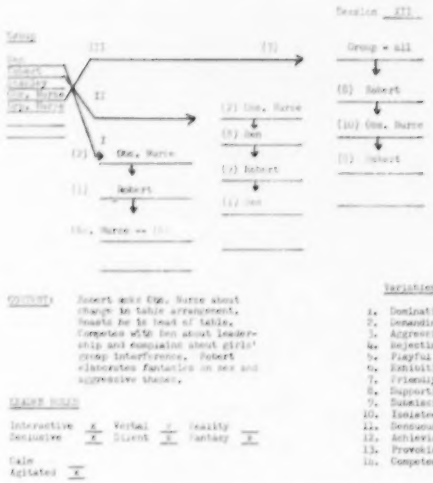

Fig. 1.—Sequential rating schema.

Expressions, (2) Passivity Level of Group; Interpersonal: (1) Pairing, (2) Group Participation, (3) Isolation, (4) Competition; Personal: (1) Affect Expressions, (2) Sensory-Body Content, (3) Egocentricity.

A three-step scale of High, Moderate, and Low was used to grade each of the participants on the above variables whenever a new theme or sustained interaction occurred. By comparing the variables that appeared significantly between the beginning and the end of each session, we could trace each member's use of the intellectual, motoric, interpersonal, or personal aspects of his defenses and thus assign causality and interpret the vectors of leadership.

Figure 2 offers an example of the final pooled ratings of these variables at the beginning and end of Session I. The "Direction" column indicates that Acting Expressions were superseded by Passivity and that Interpersonal Pairing predominated early attempts at Interpersonal Group Participation. The notation of +C assigns importance to Competition as a major variable of the interaction.

## Observations

Four boys constituted the hard, loyal, and unified core of the boys' group. They had adjusted to each other's idiosyncratic pathologies and defenses and presented a fairly stable front to newcomers. By observing their leadership and individual character adjustments to three new boys of differing personality constellations, we expected, on the one hand, to identify the predominant variables that spelled out construction or destruction of a group process and, on the other, to extend our knowledge of the individual's dynamics.

Harold, age 13, was acknowledged as the historical leader of the group. He had the second longest period of hospitalization, in which he had developed intellectual, social, and manipulative skills, such as feats of daring and the leading of revolts upon adult authority, which apparently well compensated for his frail appearance. An only and spoiled child, admitted to the unit for severe anorexia nervosa, he had a long history of respiratory-somatic complaints, thumb sucking, and temper tantrums. Psychiatric evaluation pointed to an obsessive-compulsive character disorder used defensively against aggressive orality. Psychological testing emphasized a gifted, imaginative, manipulating child with psychotic-like regressed infantile affective needs.

Robert, age 13, was well established as a member of the group at the time of the study but only after overt rejection and a very gradual acceptance. A turning point in his status occurred when he won a boxing match over Stanley. He mimicked and followed Harold's leadership with an abiding passivity, in contrast to the aggressiveness shown to personnel. He was the older of the two fraternal siblings consistently infantalized by an indulgent mother. He had a lifelong history of enuresis and thumb sucking and more recently had developed severe multiple tics and anorexia nervosa. Psychiatric examination outlined an admixture of oral and phallic defenses. Psychological consultation revealed a gross lack of ego integration and fixation at primitive oral levels.

Ben, age 10, had been passive, withdrawn, and depressed from the time of admission but had always wanted to join the group. He was humorously tolerated with such names as "Ben, the

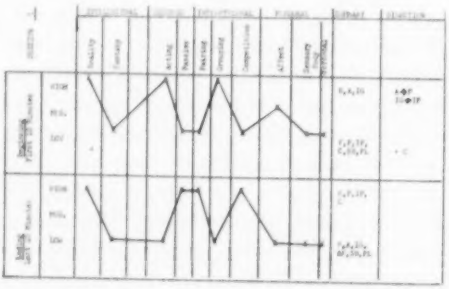

Fig. 2.—Final pooled ratings.

educated bear." He maintained membership as the passive worshiper of any strong boy, the faithful audience and supporter of surreptitious rebellions. Presenting complaints were withdrawn, fearful behavior, school phobia, lengthy gastrointestinal disorders, and depressions. A sister, 7 years his senior, had recently experienced a schizophrenic break. Psychiatric opinion classified this boy as predominantly phobic with extensive oral deprivation. Psychological material described unsuccessful attempts at compulsive defenses, elaborate symptom formation, and a borderline psychotic withdrawal.

Stanley, age 8, had been on the unit the longest. He was admitted a year and a half previously with a clinical picture of an acute paranoid schizophrenic reaction. Hyperactive and aggressive, he had paranoid delusions, principally centered about poisoned food. At the time of the study, some delusions had been replaced by compulsive ritual. He was recognized by his group as the sickest member because of his psychotic rages; yet he was accepted as a rather isolated member of the boys' group during his more quiescent periods. Psychiatric evaluation at the time of the study classified his illness as an obsessive character disorder with predominant oral regressive features. Psychological testing supported the conclusions of a reactive rather than a process schizophrenia with concomitant intense physical deprivations.

Into this admixture of defenses of reality manipulations, fantasy-oral regressions, withdrawing passivity, and psychotic rages the first new member, Norton, age 11, was introduced. Since his problems centered about a compulsive reality orientation and negativism, we expected that he would compete with Harold for some nominal control of the leadership. However, our prediction had failed to consider the indirect subtleties of Harold's power and the secondary defenses that Norton could not attempt with adults. Instead of the precocious, compulsive, reality scheduling characteristic of Norton's early days in the hospital, in the first group session he turned artfully toward the role of follower and elaborator of fantasies and acting-out expressiveness—two kinds of behavior that had not been evident in previous ward adjustments. With this new-found strength, he directly invaded the exclusively controlled fantasy domains of Robert. Robert retaliated by direct and personal criticism of Norton and his therapist, forcing Norton to alter suddenly his responses toward reality information and personal criticism. By the end of the session, leadership between Norton and Robert was divided, and the adults had been forced out of the interaction. Our group ratings indicated that this stalemate had been reached through a transition from the unstable acting techniques to a competitive interpersonal pairing. The high passivity of the remainder of the total group, as well as Harold's amused silence, emphasized that the struggle for acceptance would go on between the two contestants for his power.

In Session II, Robert exhausted his repertoire of techniques—acting, fantasy, elaboration and information, pseudoarguments with Stanley, enlisting of support of the girls' extragroup, and, finally, an overwhelming dramatized affective discharge involving hostile fantasies. Norton, who had been somewhat seduced at the beginning of the hour into fantasy elaboration, feebly attempted reality orientations but was clearly defenseless and rejected by the end of the session. The combination of high affect and fantasy plus spirited group participation appeared to be a formula to which he could not adapt. In Session III the pairing of Harold and Norton's reality orientations finally occurred. Harold had taken the time to enlist the sympathetic support of the head nurse at the beginning of the hour and then was able to squelch effectively Robert's elaborate fantasy about blowing up the hospital director's car, which ordinarily would have given the latter great group prestige. By following Harold's attack on adult reality roles, Norton was able to use his best characterological negativism and so gain nominal leadership. With Harold absent in Session IV, Robert effectively employed a combination of critical affect and immobilization of the adults with guilt-producing accusations (a favorite technique of Harold) to regain leadership and once more enforce the direct rejection of Norton. In summary, within four sessions our group ratings had allowed the identification of individual and group processes and defenses which could be tolerated and utilized for stability.

By Session V, Norton had been discharged from the hospital and the second new member, Carl, was introduced. On admission, Carl's presenting complaints were inability to read, negativistic behavior, cortical organic deficits, and slow motor development. Our predictions that organic deficit and psychomotor rigidity would make him an obvious scapegoat again proved the limitations of the individual diagnostic appraisal. Harold, again given to manipulating others to ensure his leadership, provided the stage of interaction by introducing an aggressive theme about auto accidents. Immediately, Robert and Carl began reality and fantasy elaborations, which turned quickly to personal invectives. Outfantasied and outexhibited, Carl forcefully introduced a succession of sexual, anal, and castration themes. This enlisted immediate group support through a high level of tension and affective discharge. It produced an unusual supportive pairing with the anal themes of

Stanley, eliminated both Robert and Harold from the predominant interaction, silenced adult participation, and firmly established Carl's temporary leadership. The intimacy of the sensory-body contents proved an unusually effective device for gaining control and demonstrated the positive values of a relatively primitive and rigid defense.

The pairing of Carl and Stanley persisted in Session VI, perseverating on the same successful content and forcing Robert to displace his aggression toward the adults. Harold's last appearance before hospital discharge was in Session VII. His parting offering to the group was to raise their fears concerning tape recordings he had heard about on another child service in the hospital. In reaction to this fear, and the depression resulting from the loss of the leader, the group dissolved into inactivity, and the girls' group and the adults became the active participants. Our group ratings indicated that, for the first time, there had been no transition of defense operations from beginning to end of the hour, and this in subsequent ratings proved a reliable index of lack of leadership efforts and egocentric, depressive affects predominating in the group process.

In Session VIII, despite the stimulus of the third new member, Ken, an ingenious, autistic 12-year-old boy with a history of petit mal, the lack of efforts at renewing leadership persisted. Group ratings offered the clue that child to adult pairing had become the superseding security operation, especially reflected in excessive demands for food and attention. For the first time, themes about the security of being in the hospital setting were offered. Some tendency toward reorganization of the group process was apparent in the group motivations of reducing the participation of the girls' group. By Session IX, with Robert absent, Ken made his first attempt at defining a role for himself by sharing reality topics and food with Carl. This dependency was in sharp contrast to his usual isolated, autistic behavior and provided no competition for Carl, who could reject or accept him at will by acting, affective, or content reactions. Session X produced a pairing of Stanley and Ben on fantasy themes, and this one added ingredient of effective pairing was enough to overburden Carl's brittle operations and reduce his participation to squabbles with Ken.

The return of movement in group defenses from reality to fantasy within Sessions XI and XII clearly evidences the return of the leadership contest, largely through Robert's efforts. Under a barrage of dreams, fantasies, acting, anal-power themes, and reality topics—in short, all the techniques that now had been historically effective in the formation of the group—the group acquiesced in the uncontested leadership of Robert. With one exception, this leadership persisted and, after stabilizing, produced a salutory reality orientation in all the members. It is noteworthy that during this period, even when the leader was immobilized by his predominant symptom—gross facial and gestural tics—the passivity of each of the remaining members became additive and promoted a waiting period until the leadership was again mobilized, rather than encouraging new competitive bids. Under this new tranquility of established leadership and an absence of the stimulation of new membership, no group defense movements were apparent in our ratings.

Reality dependency relations to adults and pairing with peers became the main reflectors of low tension and low cohesiveness in group relations and a reversion to more characteristic individual adjustments.

By comparing the characteristic individual patterns with the roles and defenses of group interactions, we found our knowledge could be extended in the areas of diagnostic appraisal, compatibility for group activities, and therapeutic planning.

From the standpoint of our selected variables, the *successful* ingredients for group participation, as represented in Carl, are outlined as follows: Fantasy, Motor Expressiveness, Group Interpersonal Reactions, Competition, and Highly Personalized Orientations, including direct affective reactions, sensual contents, and egocentric referents. Surprisingly, the role of competitor for secondary leadership, rigidity in defense structure, and egocentricity proved to be definite assets.

The most forceful but *relatively unsuccessful* bid for membership was represented by Norton's constellation of Reality, Pairing Interpersonal Reaction, Competition, and Egocentricity. Despite Norton's superior intellectual endowment, reality information, adaptation of defenses, and advanced ego-integrative capacities, he appeared to provide only group tension, without offering a means of affective, shared releases.

Although Ken's assets paralleled Carl's configuration, his intellectual limitations, autistic egocentricity, and pairing interpersonal tendencies made him a rejectee, who was minimally tolerated within the physical,

but not psychological, limits of the group.

An exploratory study based on a very limited number of children and conditions has little right to generalized conclusions. But, in the hope that they will be more provocative than definitive, we offer the following broad observations that seemed most pertinent to the urgency of our clinical needs:

1. Age, length of hospitalization, physical size, and psychiatric impairment do not appear to be critical or especially pertinent criteria for group placement.

2. Isolated, withdrawn children with learning disturbances, while failing leadership, can be tolerated and aided by group interactions.

3. In a group of children with gross emotional disturbances, a child with predominantly intellectual adaptations will appear maladaptive.

4. Regression is more easily tolerated by personnel and group members than is acting-out expressiveness.

5. Exhibitionism, which allows for empathic reactions, has an organizing, positive leadership value to such child groups.

6. Apparently, maladaptive individual adjustments may have complementary, adaptive functions in the group process.

7. Settings which stimulate basic need patterns, such as the feeding situation in this study, may produce diverse and representative behaviors which could be used to extend diagnostic appraisals.

Institute for Psychosomatic and Psychiatric Training and Research, Michael Reese Medical Center (16).

# Comparison of Psychological Effects of Certain Centrally Acting Drugs in Man

CONAN KORNETSKY, Ph.D.; ORETTA HUMPHRIES, B.S., and EDWARD V. EVARTS, M.D., Bethesda, Md.

A number of recent studies have emphasized that the psychological effects of a given drug are not entirely a function of the drug's more classic "pharmacological properties." On the contrary, as pointed out by Lasagna et al., "the nature of the subject and the situation in which a drug is administered are important determinants of drug effects." [1] The point of view which Lasagna has presented is supported by the results of Hill et al.[2] and of Kornetsky.[3] These investigators have demonstrated that an informal, friendly attitude by the experimenter toward the subject affects the analgesic effect of morphine, and that reaction time is not decreased when subjects are motivated by electric shock.[4] Von Felsinger et al.[5] have concluded that those subjects who respond atypically to one drug are likely to respond atypically to other drugs. The present studies have been designed to obtain further data concerning the degree to which the psychological effects of certain drugs are dependent on the reaction pattern of the subject, and, therefore, independent of the specific pharmacological activity of the drug which has elicited these effects. An attempt has been made to test the hypothesis that the magnitude of drug-induced psychological effects is significantly related to the reactivity of the subject.

In addition to obtaining data concerning the questions raised in the previous paragraph, the present studies have been designed to compare certain of the psychological effects of several classes of centrally active agents; the drugs which were selected include secobarbital, meperidine, chlorpromazine, and lysergic acid diethylamide (LSD). These drugs were selected as representatives of the categories of narcotic, hypnotic, psychotomimetic, and "tranquilizing" agents. Data were obtained concerning the extent to which these agents produce impairment of performance on certain psychomotor and intelligence tests; it seemed that such data might be of value in arriving at conclusions concerning the degree to which the impairment produced by a "tranquilizing" drug, such as chlorpromazine, might differ from impairment produced by hypnotic and narcotic drugs, such as secobarbital and meperidine.

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## Methods

Ten normal volunteers between the ages of 18 and 23 years, 6 males and 4 females, served as subjects. The subjects had had little or no previous experience with centrally acting drugs. Each subject received the following drugs at the dosages indicated: meperidine hydrochloride, 50 and 100 mg.; secobarbital sodium, 100 and 200 mg.; chlorpromazine hydrochloride, 200 and 400 mg.; LSD, 50γ and 100γ. This dosage was maintained throughout the course of the experiment, except that, at the completion of observations on four subjects, the chlorpromazine dose was reduced to 100 and 200 mg. This was necessitated by the severity of the postural hypotension produced by single 400 mg. doses of chlorpromazine. On any single testing day the subject received only one drug. There was a minimum of one day between drug administrations. The order of administration was a 10×10 Latin-square design, which included two placebos. In addition to being administered on regular experimental days, all performance tests were given to each subject prior to and at the end of the experimental period. All drugs, including placebos, were administered orally in identical capsules; the "double-blind" technique was employed throughout.

On each experimental day, as well as on the two control days, the following tests were given, starting 75 minutes after the ingestion of the drug:

1. Speed of addition (three digits)[6]
2. Speed of addition (nine digits)[6]
3. Modified digit symbol test[7,8]
4. Speed of copying numbers[6]
5. Pursuit rotor (a standard Gerbrand machine rotating at a rate of 30 rpm was used)
6. Tachistoscopic discrimination of circle size (two circles at a time were tachistiscopically (0.01 to 1.0 second's exposure) projected, and the subject was required to make a judgment as to which circle was the larger)
7. Tactual threshold determination (the skin on the index finger of the right hand was stimulated with finely graded nylon hairs, and the subject was asked to respond verbally when he felt something[10])
8. A 46-item symptom questionnaire,[11] administered to the subjects 30, 90, 150, and 210 minutes after ingestion of the drugs

An analysis of variance[12] was performed on the data for each test. The significance of the differences between the subjects' scores on each drug day and the mean of the two placebo scores was tested by the Dunnett $t$-test,[14] and the significance of differences in the effects of the drugs on the individual tests was determined by the Scheffé test.[15] In order to obtain some over-all estimate of drug effects and also to partial out the differences in original abilities of the subjects on the tests, the mean scores for each subject on each test were expressed as a percentage of the mean of his scores on the same test on the two control days. The mean of the transformed scores for all tests was obtained separately for each subject for each drug. The means for each drug were then obtained, and an analysis of variance was performed.

To determine the relationship between objective and subjective psychological effects, the strength of the relationship between the mean over-all per cent score on the objective tests and the number of positive responses on the symptom questionnaire were correlated by means of the rank-difference method ($\rho$).[13]

## Results

The analysis of variance results for each test produced a significant $F$ ratio for both drug and individual variance but no significant variance for days. The summaries of these analyses are shown in Table 1. Table 2 shows the mean scores obtained for each drug on each test. LSD had significant effects on performance on the addition test (both three and nine digits for 100/$\gamma$ of LSD), the digit symbol test, and the tachistoscopic discrimination of circle size. Two hundred milligrams of secobarbital sodium had significant effects on the digit symbol and pursuit rotor tests. Two hundred milligrams of chlorpromazine hydrochloride significantly affected performance on the digit symbol and pursuit rotor tests. With the exception of 200 mg. of secobarbital sodium, 100$\gamma$ of LSD produced significantly more impairment than any of the drugs. Two hundred milligrams of secobarbital sodium produced more impairment than LSD on the three-digit addition test. In no other test were the effects of the high doses of the drugs significantly different from one another. A more comprehensive picture of the

TABLE 1.—*Summary of Analyses of Variance for All Tests*

| | | Addition (3 Digits) | | Addition (9 Digits) | | Speed of Copying | | Digit Symbol Test | |
|---|---|---|---|---|---|---|---|---|---|
| Source of Variance | *df* | Mean Sq. | *F* | Mean Sq. | *F* | Mean Sq. | *F* | Mean Sq. | *F* |
| Individuals | 9 | 6824.68 | 71.2* | 2829.70 | 62.1* | 3118.76 | 27.5* | 967.14 | 24.6* |
| Drugs | 9 | 738.78 | 7.7* | 342.60 | 7.5* | 241.91 | 2.1† | 425.16 | 10.8* |
| Days | 9 | 175.40 | 1.8 | 47.69 | 1.1 | 73.47 | 0.6 | 68.44 | 1.7 |
| Residual | 72 | 95.88 | | 45.58 | | 113.37 | | 39.28 | |
| Total | 99 | | | | | | | | |

| | | Pursuit Rotor | | Visual Discrimination | | Tactual Perception | |
|---|---|---|---|---|---|---|---|
| Source of Variance | *df* | Mean Sq. | *F* | Mean Sq. | *F* | Mean Sq. | *F* |
| Individuals | 9 | 216.75 | 23.8* | 690.98 | 83.9* | 182.17 | 7.6* |
| Drugs | 9 | 97.21 | 10.7* | 24.69 | 3.0* | 71.80 | 3.0* |
| Days | 9 | 10.42 | 1.1 | 5.98 | 0.7 | 20.06 | 0.8 |
| Residual | 72 | 9.10 | | 8.24 | | 24.03 | |
| Total | 99 | | | | | | |

* $P < 0.01$.
† $P < 0.05$.

TABLE 2.—*Mean Raw Score for Each Drug on Each Test*

| | LSD | | Meperidine | | Secobarbital | | Chlorpromazine* | Placebo | |
|---|---|---|---|---|---|---|---|---|---|
| | 50 γ | 100 γ | 50 Mg. | 100 Mg. | 100 Mg. | 200 Mg. | 200 Mg. | 1 | 2 |
| Addition (2 digits), digits per min. | 64.5† | 60.4† | 77.9 | 74.2 | 75.4 | 66.3 | 76.1 | 74.1 | 75.5 |
| Addition (9 digits), digits per min. | 37.6 | 25.0† | 42.3 | 41.9 | 44.5 | 37.0 | 39.6 | 42.6 | 42.1 |
| Speed of copying, digits per min. | 86.7 | 75.6 | 84.4 | 84.4 | 85.0 | 73.6† | 74.8 | 86.1 | 84.2 |
| Digit symbol, total correct | 53.0 | 41.1† | 59.6 | 56.4 | 55.3 | 49.9† | 50.0† | 57.1 | 58.3 |
| Pursuit rotor, sec. | 19.2 | 18.5 | 22.0 | 19.7 | 19.6 | 15.6† | 15.9† | 20.1 | 21.5 |
| Visual discrimination, incorrect | 9.3 | 10.8† | 6.3 | 7.6 | 7.0 | 9.4 | 7.8 | 6.5 | 6.5 |
| Tactual perception, no. correct | 53.3 | 51.7 | 55.6 | 57.5 | 56.3 | 52.8 | 52.8 | 56.5 | 52.9 |

* Since only six subjects received 100 mg. and only four received 400 mg., these results are not reported on the individual tests.
† $P<0.05$ (between score and mean of two placebos).

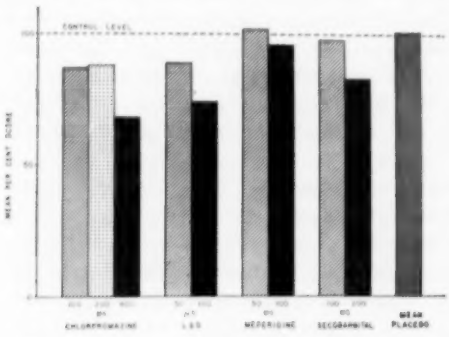


Fig. 1.—Mean per cent over-all score for each drug.

comparative effects of the drugs is shown in Figure 1. The summary of the analysis of variance for these data is shown in Table 3.

Since it was not expected that any of the drugs would produce an over-all increase in performance, single-tailed Dunnett *t*-tests were employed to determine the significance of the difference between the effects of each drug and of the mean of the two placebos. The effects of 200 mg. of secobarbital sodium; 100, 200, and 400 mg. of chlorpromazine hydrochloride, and 50γ and 100γ of LSD differed significantly from those of the placebos ($P<0.05$). High doses of secobarbital, meperidine, LSD, and chlorpromazine produced more impairment than low doses of the same drugs ($P<0.05$).

An analysis of the effects of the three doses of chlorpromazine (6 subjects received 100 mg.; 10 received 200 mg., and 4

TABLE 3.—*Summary of the Analysis of Variance for Over-All Per Cent Scores*

| Source of Variance | *df* | Sum Sq. | Mean Sq. | *F* | *F* |
|---|---|---|---|---|---|
| Tests | 6 | 2.130 | 0.3550 | $\frac{T}{T\times S}$ | 2.58* |
| Drugs | 8 | 6.591 | 0.8239 | $\frac{D}{D\times S}$ | 10.06† |
| Subjects | 9 | 3.280 | 0.3644 | $\frac{S}{D\times S\times T}$ | 12.23† |
| Tests×drugs | 48 | 5.082 | 0.1059 | $\frac{D\times T}{D\times S\times T}$ | 3.55† |
| Drugs×subjects | 72 | 5.927 | 0.0819 | $\frac{D\times S}{D\times S\times T}$ | 2.75† |
| Subjects×tests | 54 | 7.419 | 0.1374 | $\frac{S\times T}{D\times S\times T}$ | 4.61† |
| Drugs×subjects×tests | 432 | 12.867 | 0.0298 | | |
| Total | 629 | 43.296 | | | |

* $P<0.05$.
† $P<0.01$.

received 400 mg.) by means of the *t*-test showed that 400 mg. of chlorpromazine hydrochloride produced significantly more impairment of performance, at ($P<0.01$), than did 200 mg. on speed of addition (three and nine digits), digit symbol, pursuit rotor, visual discrimination, and tactual threshold tests. Two hundred milligrams of chlorpromazine hydrochloride produced a significantly greater degree of impairment in performance than did 100 mg. on only the digit-symbol test ($P<0.05$).

The analysis of the responses to symptom questionnaire (mean number of symptoms for four periods after receiving the drug) is summarized in Figure 2; the analysis of variance is shown in Table 4. Although all the drugs produced an average increase in reported symptoms, only 50γ and 100γ of LSD, 200 mg. of secobarbital sodium, and 400 mg. of chlorpromazine hydrochloride produced a statistically significant increase in the number of symptoms over the mean for the two placebos.

Table 5 presents the results of the correlation of the over-all objective scores and the subjective scores (symptom questionnaire) for each drug. As the data indicate, there was no significant correlation of the objective effects and the subjective effects

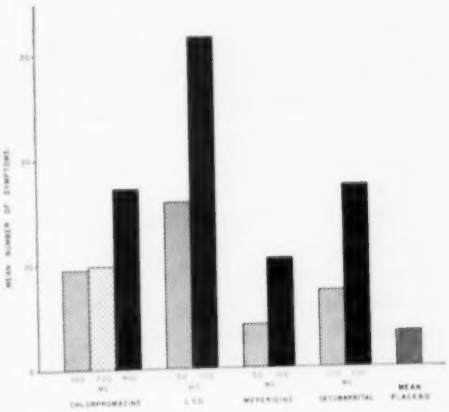

Fig. 2.—Mean number of symptoms on the symptom questionnaire for each drug.

of any one of the drugs taken individually, with the exception of 200 mg. of secobarbital sodium. One hundred micrograms of LSD produced a negative, but not significant, correlation (the greater the subjective effect, the less marked the objective effects). However, the mean objective effects correlate with the mean subjective effects ($\rho=0.84$) for all drugs at a statistically significant level. Thus, there is no discrepancy between objective and subjective effects when a correlation between drugs rather than between subjects is computed.

TABLE 4.—*Summary of the Analysis of Variance for the Symptom Questionnaire*

| Source of Variance | *df** | Sum Sq. | Mean Sq. | *F* |
|---|---|---|---|---|
| Drugs | 7 | 5,891.4 | 844.628 | 16.50† |
| Subjects | 9 | 1,031.2 | 114.577 | 2.25‡ |
| Residual (D×S) | 63 | 3,212.65 | 50.994 | |
| Total | 79 | 10,135.25 | | |

* The smaller number of degrees of freedom in this analysis was due to the combining of the two placebos and the use of only 200 mg. of chlorpromazine.
† $P<0.01$.
‡ $P<0.05$.

TABLE 5.—*Correlations (ρ) Between Objective (Over-All Score) and Subjective (Symptom Questionnaire) Effects of the Various Drugs*

| Placebo* | LSD | | Meperidine | | Secobarbital | | Chlorpromazine |
|---|---|---|---|---|---|---|---|
| | 50 γ | 100 γ | 50 Mg. | 100 Mg. | 100 Mg. | 200 Mg. | 200 Mg. |
| 0.46 | 0.39 | −0.36 | −0.03 | 0.12 | 0.53 | 0.66† | 0.54 |

* Mean of two placebos.
† $P<0.05$.

## Comment

Although most of the drugs produced impairment in performance of the tests used in the present study, the large individual variability resulted in statistically significant impairment of performance on only a few tests by each drug.

Since LSD affected performance on more tests than any of the other drugs, it was somewhat surprising to find that it did not significantly affect performance on the pursuit rotor test. This suggests that LSD has little effect on motor coordination but has considerable effect on perceptual and intellectual processes. However, chlorpromazine (200 mg. or less) and secobarbital do not seem to affect simple intellectual tasks (speed of addition) but do affect more complex intellectual tasks (digit symbol test) and motor coordination (pursuit rotor). The over-all analysis of variance suggests that the drug-test interactions are significant (Table 3, Test×drugs, $F=3.55$). In studies by Abramson [16] and Jarvik and their associates,[17] it was found that LSD at doses up to 100γ did not significantly affect performance on the pursuit rotor, hand steadiness, or manual reaction time. Verbal reaction time (time to read a series of words), attention, and concentration were significantly affected by the same doses of LSD. An opposite result was reported by Landis and Clausen.[18] They found impairment of performance on some motor tests, but they did not find impairment of flicker-fusion threshold in schizophrenics after LSD. There have been no reported studies of the effects of secobarbital on the tests employed in the present study; however, some studies on the effects of amobarbital indicate that at low dose levels there is very little effect on intellectual functioning (Arkola [19] and Slater and Sargant [20]), but greater effect on motor performance as measured by reaction time and the tracing of a pathway with stylus (Hill and Belleville [21]). Although secobarbital did not significantly affect visual discrimination in the present study, Ideström [22] has reported that moderate (0.30 gm/70 kg. of body weight) single doses of barbiturates produce an increase in the flicker-fusion threshold. It is unlikely that flicker fusion and discrimination for circle size measure the same aspect of visual function. The results obtained with chlorpromazine in the present study are in opposition to the findings of Lehmann and Hanrahan,[23] who reported that chlorpromazine in doses large enough to produce somnolence had no detrimental effect on a variety of psychological tests.

The analysis of variance of the over-all mean per cent scores (Table 3) gave a significant $F$ ratio for all the sources of variance. The significant subject variance suggests that those subjects whose performance was most impaired by one drug are those whose performance was most impaired by the other drugs. However, this subject responsivity is not linear, since the drug×subject interaction was also significant. To test the extent of this responsivity or reaction pattern of the subjects, the Kendall coefficient for concordance was computed.[24] This yielded slight but positive evidence for the presence of a phenomenon of this type ($w=0.35$; $P<0.01$ level). This was also true, but to a less degree, for the symptom questionnaire data. ($w=0.26$; $P<0.05$ level). These results indicate that there is some factor independent of the drug, as well as some factor dependent on an interaction with specific drugs, which accounts for a portion of the total variance. This factor may be a function of personality, as suggested by von Felsinger, Lasagna, and Beecher, or it may be a function of specific pharmacological sensitivity and/or other physiological differences on the part of individual subjects.

The importance of placebo effects in the study of drugs has been emphasized by many investigators. However, in the present experiment the results of the tests done after administration of a placebo showed no significant placebo effect. The results obtained on the symptom questionnaire were an exception in that on this subjective test

there were a number of positive responses following placebo administration. Since the symptom questionnaire was not administered during the control period, the responses of placebo-treated subjects to the symptom questionnaire could not be interpreted as placebo effects.

The significant correlation between objective and subjective effects of the drugs indicates that the drugs which caused the greatest objective impairment in functioning also had the most marked subjective effects. However, the general lack of significant correlation between subjective and objective effects produced by each drug in the individual subjects (Table 5) indicates that, although a subject may feel he is greatly affected by a drug, there may be little or no actual impairment in his functioning. The opposite also holds true; many of the subjects who did not show drug effects on the symptom questionnaire were greatly impaired in their ability to carry on the tests. This suggests that there may be a dichotomy between the objective and subjective effects of a drug, making it impossible to predict accurately the extent of one type of effect from the extent of the other.

It is of interest that of the four drugs studied meperidine was the only one that produced pleasant effects in the majority of subjects. Many of the subjects said they would like to receive that "pleasant" drug again. Most of the subjects found that 200 mg., or more, of chlopromazine and 100γ of LSD produced unpleasant effects. The chlorpromazine made them feel faint, nauseated, dizzy, and very sleepy. The LSD made them feel anxious, tense, and in some instances depressed.

## Summary

Ten normal volunteers were given various doses of lysergic acid diethylamide (LSD), meperidine, secobarbital, and chlorpromazine. The order of drug administration was a 10×10 Latin square, which included two placebos.

All drugs were administered orally, and the "double-blind" technique was employed throughout. Seventy-five minutes after ingesting the drug, subjects were given a variety of psychological tests, which included intellectual, motor, and perceptual tasks.

The following conclusions were drawn from the data:

The effects of drugs on psychological performance in man are due not only to the specific pharmacological activity of the drug, but also to the specific reactivity of the subject and to an interaction of the two.

There is not a significant correlation between the objective and the subjective psychological effects of a given drug. However, the drugs that produce the greater mean objective effect also produce the greater mean subjective effect.

Two hundred milligrams of secobarbital sodium; 100, 200, and 400 mg. of chlorpromazine hydrochloride, and 50γ and 100γ of lysergic acid diethylamide significantly impair performance on a variety of psychological tests. Meperidine hydrochloride in 50 and 100 mg. doses does not impair performance on the same psychological tests.

LSD had significant effects on intellectual and perceptual tasks but did not cause significant impairment of motor tasks, whereas chlorpromazine and secobarbital affected motor tasks but in general did not cause statistically significant impairment of performance on simple intellectual and perceptual tasks.

Two hundred milligrams of chlorpromazine does not impair performance significantly less than does 200 mg. of secobarbital sodium.

Dr. Seymour Geisser and Mr. Samuel W. Greenhouse, of the Experimental Statistics Section, National Institute for Mental Health, assisted in the statistical analysis of the data.

Laboratory of Clinical Science, National Institute of Mental Health (14).

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# Relationship Between Effects of a Number of Centrally Acting Drugs and Personality

CONAN KORNETSKY, Ph.D., and OGRETTA HUMPHRIES, B.S., Bethesda, Md.

The relationship between the effects of drugs and the personality of the recipient of the drugs is an area of research that has been ignored, for the most part. It is usually tacitly assumed that the personality will have something to do with the manner in which the individual responds to a drug. This view is commonly held concerning alcohol. Most people who have observed others under the influence of this drug are implicitly, if not explicitly, aware that the personality of the indulger, as well as the situation, will contribute to the effect of this universal relaxer.

A specific attack on the problem of the relationship between personality and drug effect was made by von Felsinger, Lasagna, and Beecher.[1] They concluded that those subjects who seemed to have deviant personalities, as determined by interview and the Rorschach test, were the subjects who responded atypically to amphetamine and morphine. These investigators stated explicitly[2] that the effects of a drug are determined not merely by the specific pharmacological action of the drug, the dose, and the route of administration, but also by the nature of the subject and the situation in which the drug is given.

The present report is part of a larger study[3] which compared certain of the psychological effects of several classes of centrally acting agents. The following drugs and dosages were used: secobarbital sodium, 100 and 200 mg.; meperidine hydrochloride, 50 and 100 mg.; chlorpromazine hydrochloride, 100, 200, and 400 mg., and lysergic acid diethylamide (LSD), 50γ and 100γ. The original design called for subjects to receive 200 and 400 mg. of chlorpromazine; however, owing to the severity of postural hypotension, this was reduced to 100 and 200 mg. after the higher doses were given to the first four subjects. These compounds were selected as representative of the categories of hypnotic, narcotic, "tranquilizing," and psychotomimetic drugs. The subjects used were 10 normal volunteers between the ages of 18 and 23, 6 males and 4 females. There was a minimum of one day between drug administrations, and the order of administration was a 10×10 Latin square which included two placebos. All drugs, including placebos, were given orally in identical capsules; the "double-blind" technique was employed throughout.

The tests used to measure the effects of these drugs were as follows: addition, both three and nine digits; pursuit rotor; digit symbol test; speed of copying numbers; tachistoscopic discrimination, and tactual perception. Scores were expressed as a per cent of the mean of two control scores, and then an over-all mean per cent score for all tests was obtained. This score will be referred to as the objective test score.

In addition to receiving the objective tests, each subject received a 46-item questionnaire at 30, 90, 150, and 210 minutes after the ingestion of the drug. The score on this questionnaire (the total number of symptoms for the four periods) will be referred to as the subjective score.

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The results of the above study indicated that the psychological effects of these drugs are somewhat dependent on the reaction pattern of the subject, and independent of the specific pharmacological activity of the drug which elicited the effects. Thus it was found that those subjects who were most affected by one drug were also most affected by the other drugs.

## Present Report

The present report deals with the correlations between four MMPI (Minnesota Multiphasic Personality Inventory[4]) scales and the extent of effect of each of those drugs that significantly altered the objective and subjective responses. An a priori decision was made to use only the Hy (hysteria), and Hs (hypochondriasis), D (depression), and Pt (psychoasthenia) scales from the MMPI. The Hy and Hs scales were selected because it was believed that these might very well correlate with both placebo and drug effects; the D scale, because of our impression, based on other studies, that the more depressed a person was the greater the effect of the drugs, and the Pt scale, because it was believed that this was a good measure of general anxiety level. The Pt scale is significantly correlated (0.92) with the Taylor Scale of Manifest Anxiety.[5] The MMPI was administered prior to the start of the experiments.

TABLE 1.—*Rank-Difference Correlations (ρ) Between MMPI Scales and Subjective Effects of Centrally Acting Drugs*

| | MMPI Scale | | | |
|---|---|---|---|---|
| Drug | Pt | D | Hs | Hy |
| Secobarbital, 200 mg. | 0.58 | 0.66 | 0.16 | 0.16 |
| Chlorpromazine, 200 mg. | 0.73 | 0.57 | 0.56 | 0.49 |
| LSD, 50 γ | 0.94 | 0.57 | 0.46 | 0.47 |
| LSD, 100 γ | 0.14 | 0.10 | −0.11 | 0.08 |
| Placebo | 0.01 | 0.00 | 0.06 | 0.10 |

## Results

Table 1 shows the rank-difference correlations[6] between each of the four MMPI scales and the effects of those drugs that produced significant or near-significant effects on the subjective data. Although 400 mg. of chlorpromazine hydrochloride produced a significant increase in plus responses, the computation of a correlation was precluded, for only four subjects received this large a dose.

TABLE 2.—*Rank-Difference Correlations (ρ) Between MMPI Scales and Objective Effects of Centrally Acting Drugs*

| | MMPI Scale | | | |
|---|---|---|---|---|
| Drug | Pt | D | Hs | Hy |
| Secobarbital, 200 mg. | 0.31 | 0.60 | 0.20 | 0.42 |
| Chlorpromazine, 200 mg. | 0.53 | 0.15 | 0.14 | 0.14 |
| LSD, 50 γ | 0.51 | 0.56 | 0.25 | 0.45 |
| LSD, 100 γ | 0.24 | 0.47 | 0.59 | 0.23 |
| Placebo | 0.59 | 0.27 | 0.06 | 0.03 |

Table 2 shows the rank-difference correlations between each of the four MMPI scales and the objective psychological data.

In both Tables the larger the correlation the greater the relationship between the extent of drug effect and deviation in the personality scale.

## Comment

The scores on the psychoasthenia and depression scales showed significant, or almost significant, relationships with the subjective effects of 200 mg. of secobarbital sodium, 50γ of LSD, and 200 mg. of chlorpromazine hydrochloride. Thus, the more deviant the subject on these two MMPI scales, the greater were the subjective effects of these drugs.

The failure of the subjective effects of 100γ of LSD to show any relationship with MMPI, while the effect of 50γ was significantly related to the MMPI scores, suggests that when a severe drug effect is obtained, the personality of the subject does not play an important role. In other words, if a large enough dose of any drug were given, all subjects would respond in the same manner. The lack of a relationship between the placebo effect and personality was somewhat contrary to what might be expected, for here the drugs exert no influence on the performance of the subjects. The subject has the possibility of allowing his personality to account for all of the variance.

The correlations between the Pt and D scales and the objective drug effects also yield positive relationships. However, these correlations were not as large as those between the subjective effects and the MMPI scales. The relationships between the ob-

jective effects and the Hy and Hs scales were smaller than those with the Pt and D scales. However, the effects of 100γ of LSD did correlate almost significantly with the Hs scale.

The conclusions that can be arrived at from these results must be somewhat circumscribed, for the number of correlations computed would give some significant correlations by chance alone. In addition, there was no specific hypothesis as to the relative extent of relationship between each drug and the specific MMPI scale. There was the the general hypothesis, however, that in the case of those drugs that produced significant effects on the tests used, there would be a positive relationship with the score on some of these MMPI scales. In other words, the more deviant a subject on the MMPI scales the greater the drug effect. This hypothesis is believed to be supported by the data.

The results of this investigation, along with those from the previous report,[3] indicate that there are reactors and nonreactors to drugs and that the reactors are likely to be those people who are more depressed (the D scale) and/or likely to have more unreasonable fears of things, as well as overreact to environmental stimuli (the Pt scale).

It must be mentioned that there are physiological factors that also contribute to the responsivity of people. In further studies these variables will be investigated.

## Summary

Ten normal young adults were given various doses of chlorpromazine, meperidine, secobarbital, and lysergic acid diethylamide (LSD). The effects of the drugs were determined by both objective and subjective psychological tests. The Minnesota Multiphasic Personality Inventory was also administered to all the subjects prior to the start of the experiment. Four scales from this test were selected for testing relationships between personality variables and both the objective and the subjective effects of the drugs.

The Depression and Psychoasthenia scales correlated significantly, or almost significantly, with the subjective effects and, to a less extent, with the objective effects of those drugs and dosages that produced significant effects.

These results support a hypothesis that personality plays a role in determining the extent of drug effect.

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# Effects of Centrally Acting Drugs on Two Tests of Brain Damage

DANIEL W. PRIMAC, M.A.; ALLAN F. MIRSKY, Ph.D., and H. ENGER ROSVOLD, Ph.D., Bethesda, Md.

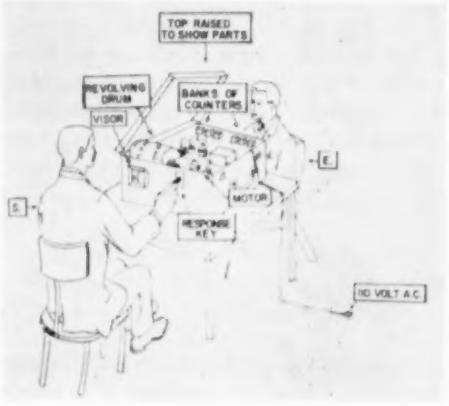
The purpose of the present investigation was to measure the effects of several centrally acting drugs on the performance of tasks designed primarily for studying the effects of brain damage. The tasks employed were the Continuous Performance Test[1] and the Wisconsin Card Sorting Test.[2] The Continuous Performance Test (C. P. T.), designed to measure sustained attention, is essentially a visual discrimination task, in which the subject must respond within short periods of time to briefly presented stimuli. In general, brain-damaged subjects perform more poorly on it than do non-brain-damaged controls. The Wisconsin Card Sorting Test was designed by Grant and Berg to provide quantitative measures of the kind of rigid and concrete performance that brain-damaged persons display on the Weigl-Goldstein-Scheerer[3] Color Form Sorting Test. A comparison on these tests of the effects of brain damage and the effects of centrally acting drugs, especially when the locus of action in the central nervous system of these drugs is considered, may aid in the specification of the locus in the brain of the functions involved in these tests.

## Methods

*Subjects and Procedure.*—The subjects, drugs, and design of the experiment were identical with those described by Kornetsky et al.[4]; after a subject had finished taking the test battery used by Kornetsky, he was tested immediately afterward, on the same day, with the C. P. T. and the Wisconsin Card Sorting Test. The subjects were tested on the average of three and a half hours after the administration of the drug, with a range of two to five hours. To review the procedure briefly, the subjects, whose mean age was 20.5 years and whose mean Wechsler-Bellevue Verbal I. Q. was 110.3, included six males and four females. They were tested after oral administration of one of four different drugs at two dose levels or one of two placebo treatments, according to a Latin-square design. The drugs and doses used were chlorpromazine hydrochloride, 200 and 400 mg. (after the first four subjects, this dose was reduced to 100 and 200 mg.); meperidine hydrochloride, 50 and 100 mg.; lysergic acid diethylamide (LSD), 50γ and 100γ, and secobarbital sodium, 100 and 200 mg.

*Tests.*—The C. P. T. (Fig. 1) consists of two tasks, the X task, in which the subject depresses a response key whenever he sees the letter *X* pass by in the visor, and the AX task, in which he depresses the key whenever he sees an *X* follow immediately after the letter *A*. Letters, mounted on the circumference of the revolving drum, appear at the rate of about one per second. A 10-minute record of the subject's performance on each task (X and AX) is scored in two ways:

Fig. 1.—Semischematic view of the Continuous Performance Test.

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Section on Animal Behavior, Laboratory of Psychology, National Institute of Mental Health, National Institutes of Health, U. S. Public Health Service, Department of Health, Education, and Welfare.

(1) the relative score, defined as the number of correct responses divided by the total number of responses the subject has made, and (2) the absolute score, defined as the number of correct responses divided by the total number of correct responses possible. Since there are 160 *X*'s presented in the X task, there are 160 possible correct responses. Similarly, there are 120 possible correct responses on the AX task. Thus, the C. P. T. yields four scores: X-Relative, X-Absolute, AX-Relative, and AX-Absolute.

Seven measures were used in scoring the Wisconsin Card Sorting Test. These were (1) the number of categories sorted, (2) the total number of errors, (3) the grand total number of errors in the first six categories, (4) the total number correct, (5) the total number of perseverative errors, (6) the total number of nonperseverative errors, and (7) the total number of unique errors.

## Results

*Wisconsin Card Sorting Test.*—Because 6 of the 100 tests (10 subjects×10 conditions) with the Wisconsin Card Sorting Test were missed, these data could not be analyzed by means of analysis of variance. However, the performance of the subjects was analyzed using nonparametric tests, which showed no significant change due to drugs in any of the seven measures used.

*Continuous Performance Test.*—The results of the analysis of variance on the C. P. T. measures are presented in Table 1. The variance due to individuals was significant ($P<0.01$) in all four C. P. T. measures. The variance due to days (order of administration) was not significant in any of the tasks. The variance due to drugs was significant at the 1% level on all of the measures except the AX-Relative ($P<0.20$).

To investigate the source of the significant drug variance, the mean score on each C. P. T. measure for each drug was compared with the placebo mean, using Dunnett's *t*-test.[5] Table 2 presents the mean percentage of the four C. P. T. measures for the 10 subjects under low and high doses of the four drugs and the placebo. The only drug for which the scores differed from the placebo was chlorpromazine; in this analysis only the 200 mg. dose scores were used. The scores were significantly lower on the X-Relative ($P<0.01$), the X-Absolute ($P<0.01$), and the AX-Absolute ($P<0.05$).

A further analysis was made, comparing the subjects' performance on the high and the low doses of chlorpromazine. Because of the change of dosage with chlorpromazine, i. e., four subjects receiving doses of 200 and 400 mg. and six receiving doses of 100 and 200 mg., separate analyses were made for each dose combination. Figure 2 presents the mean scores of the four subjects who received 200 and 400 mg. of chlorpromazine. Performance was significantly worse with 400 mg. than with 200 mg. on the X-Absolute ($P<0.01$), X-Relative ($P<0.05$), and AX-Absolute ($P<0.01$) scores. The difference, although in the same direction, was not significant on the AX-Relative score ($P<0.20$). Figure 3 presents the mean scores of the six subjects who received 100 and 200 mg. of chlorpromazine. Performance on all four tasks of the C. P. T. was significantly worse with the high dose than with the low dose. All differences were significant at $P<0.01$, except for AX-Relative ($P<0.05$).

TABLE 1.—*Analysis of Variance, C. P. T. Measures*

| Source of Variance | *df* | X-R | | X-A | | AX-R | | AX-A | |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean Sq. | *F* | Mean Sq. | *F* | Mean Sq. | *F* | Mean Sq. | *F* |
| Days | 9 | 155.52 | 1.41 | 190.18 | 1.06 | 41.56 | 0.54 | 225.55 | 1.45 |
| Subjects | 9 | 1862.01 | 16.92* | 2404.31 | 13.46* | 1753.0 | 22.97* | 3128.53 | 20.14* |
| Drugs | 9 | 487.72 | 4.43* | 1109.89 | 6.21* | 147.74 | 1.93 | 836.22 | 5.38* |
| Residual | 71 | 110.06 | | 178.64 | | 76.64 | | 155.36 | |
| Total | 98 | | | | | | | | |

* = $P<0.01$.

TABLE 2.—*Mean C. P. T. Percentage Correct Scores for Placebo and Drug Conditions*

| Drug Dose | Placebo, Mean | Chlorprom. 200 Mg. | LSD | | Secobarbital | | Meperidine | |
|---|---|---|---|---|---|---|---|---|
| | | | 50 γ | 100 γ | 100 Mg. | 200 Mg. | 50 Mg. | 100 Mg. |
| X-R | 93.45 | 78.60 | 87.5 | 83.7 | 95.7 | 87.4 | 90.7 | 94.3 |
| X-A | 91.40 | 71.60 | 87.2 | 81.5 | 96.4 | 85.6 | 87.7 | 92.9 |
| AX-R | 90.7 | 85.20 | 84.9 | 84.4 | 93.5 | 88.3 | 92.0 | 92.9 |
| AX-A | 85.8 | 72.20 | 79.6 | 75.6 | 91.6 | 85.6 | 87.8 | 88.6 |

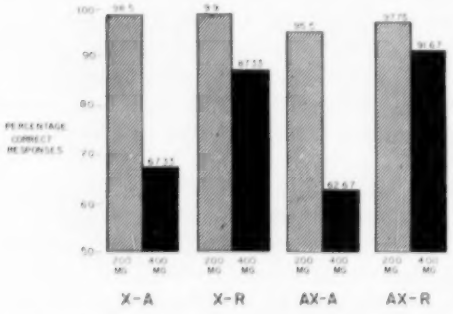


Fig. 2.—C. P. T. performance of subjects under chlorpromazine hydrochloride, 200 and 400 mg. doses.

## Comment

Of the four drugs used, only chlorpromazine, when compared with the placebo, had the effect of lowering significantly scores on the C. P. T. measures. In addition, performance under a high dose of chlorpromazine was significantly poorer than performance under a low dose in two separate groups of subjects administered two different dose combinations. The significant individual variation found in the analysis of all four C. P. T. measures seems to be in agreement with reports[6] that the threshold of tolerance for chlorpromazine differs from individual to individual.

Since only chlorpromazine produced a deficit on the C. P. T., and since there is evidence indicating that chlorpromazine probably acts to depress the reticular activating system[6-12] (although there is some evidence to the contrary[13-15]), it is possible that the C. P. T. may be sensitive to interference with the functioning of the reticular system. Because dysfunction in this system is evident in the inability of the subject to remain awake, alert, or attentive,[16-21] the impaired performance on the C. P. T. may be interpreted as an inability to maintain sustained attention.

Although chlorpromazine was the only drug in this study which significantly impaired C. P. T. performance, it is likely that some of the drugs used were not being tested at or near the time of their peak effects. Since the subjects were given the C. P. T. on the average of three and a half hours after drug administration, chlorpromazine, which has a duration of effect of approximately 6-12 hours,[22] and LSD, which has a duration of effect of from 1 to over 5 hours,[23] were undoubtedly still quite effective at the time of testing. On the other hand, the peak effect of secobarbital in the doses used is at approximately 30 minutes to 2 hours after administration.[24] Although many of the subjects slept for most of the day after receiving secobarbital, it is doubtful that the maximal effects of this drug were being measured. Similar considerations apply to meperidine, which is apparently most effective 20 to 60 minutes after oral

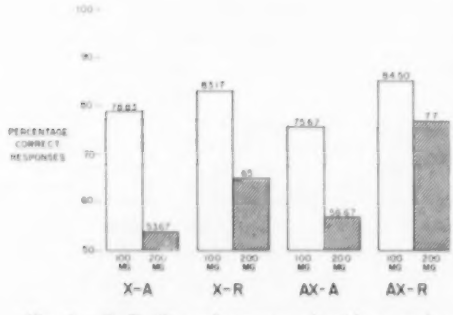


Fig. 3.—C. P. T. performance of subjects under chlorpromazine hydrochloride, 100 and 200 mg. doses.

administration.[22] In view of these considerations, it will be necessary to repeat the experiment with each drug being tested at the time of its peak effect. If under these conditions these drugs continue to have no effect, then the conclusions will be strengthened that the C. P. T. is sensitive to changes in the functioning of the reticular system and that the C. P. T. provides a test of continuous attention.

## Summary

Ten subjects, with a mean age of 20.5 and a mean verbal I. Q. of 110.3, were given low and high doses of one of four drugs or a placebo. Chlorpromazine, LSD-25, meperidine, and secobarbital were administered according to a Latin-square experimental design. The subjects were tested approximately three and a half hours after drug administration on two procedures used for assessing brain damage: the Continuous Performance Test (C. P. T.) and the Wisconsin Card Sorting Test.

None of the measures of performance on the Wisconsin Card Sorting Test show any apparent effect of the drugs. Performance on the C. P. T., however, is significantly poorer under chlorpromazine and becomes even worse as the dose is increased. Although no other drug had a significant effect on C. P. T. performance, it is doubtful that the peak effects of meperidine and secobarbital were measured.

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# Imprinting and the Establishment of Gender Role

JOHN MONEY, Ph.D.; JOAN G. HAMPSON, M.D., and JOHN L. HAMPSON, M.D., Baltimore

## Introduction

Psychologic study of hermaphrodites sheds some interesting light on the venerable controversy of hereditary versus environmental determinants of sexuality in its psychologic sense.

Human hermaphrodites of whatever variety are persons born with some degree of sexual ambiguity, anatomically and physiologically. Since they are neither exclusively male nor exclusively female, hermaphrodites are likely to grow up with contradictions existing between the sex of assignment and rearing, on the one hand, and various physical sexual variables, singly or in combination, on the other. These physical sexual variables are five in number, namely, (1) chromosomal sex, (2) gonadal sex, (3) hormonal sex and pubertal feminization or virilization, (4) the internal accessory reproductive structures, and (5) external genital morphology.

In view of the various ambisexual contradictions that may be found in hermaphroditism, one may ask whether the gender role and orientation that a hermaphrodite establishes during the course of growing up is concordant with the sex of assignment and rearing, or whether it is predominantly concordant with one or another of the five physical sexual variables.

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From the Department of Psychiatry, The Johns Hopkins University School of Medicine.

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## Psychologic Studies

During the past five years, we have investigated the sexual psychology of 105 hermaphroditic patients[1-5] of different diagnostic varieties and of all ages. The majority of them were, after their initial hospital appearance, followed from year to year. From observational notes, recorded interviews, and formal psychological tests, we obtained enough data from these patients to be able to appraise their gender role and orientation as masculine, as feminine, or as ambiguous. It was then possible to compare the gender role and orientation that each patient had established with the sex which had been assigned in infancy and in which the patient had subsequently been reared. It was also possible to compare the gender role and orientation with each of the five physical variables of sex, taken severally.

The resulting comparisons demonstrated that the sex of assignment and rearing is consistently and conspicuously a more reliable prognosticator of a hermaphrodite's gender role and orientation than is the chromosomal sex, the gonadal sex, the hormonal sex, the accessory internal reproductive morphology, or the ambiguous morphology of the external genitalia. There were only 5 among the 105 patients whose gender role and orientation was ambiguous and deviant from the sex of assignment and rearing. By contrast, for each of the five physical sexual variables, there were between 23 and 30 patients—not always the same persons*—whose sex of assignment and rearing was incongruous. In some patients this incongruity involved only one physical variable, but in most of the patients more than one physical variable was involved. Thus, some patients were predominantly female with respect to the

* The individual patients represented in each of the five tables, one for each physical variable of sex, were not identical, owing to the inconsistencies of physical contradictions in hermaphroditism; but some patients required entering in more than one table.

physical variables of sex but, having been reared as boys, had the sexual psychology of a boy, or man—and vice versa for patients reared as girls.

The clinching piece of evidence concerning the psychologic importance of the sex of assignment and rearing is provided when, among persons of identical physical diagnosis, some are reared as boys, some as girls. It is indeed startling to see, for example, two children with female hyperadrenocorticism in the company of one another in a hospital playroom, one of them entirely feminine in behavior and conduct, the other entirely masculine, each according to upbringing. As a social observer, one gets no suspicion that the two children are chromosomally and gonadally female, for psychologically they are entirely different.

Further supportive evidence concerning the importance, psychologically, of the sex of assignment and rearing is provided by cases of reassignment of sex by edict. Among our cases there were 14 patients who underwent a reassignment of sex after the early neonatal weeks. Of these 14, there were 9 below the age of 2 years 3 months at the time of the change; with 3 exceptions, they appeared subsequently to have negotiated the change without even mild signs of psychologic nonhealthiness. By contrast, only one of the five children older than 2 years 3 months at the time of reassignment of sex could possibly be rated as psychologically healthy. One infers that once a person's gender role begins to get well established, an attempt at its reversal is an extreme psychologic hazard. Psychologic nonhealthiness was markedly less common in patients without a history of sex reassignment than in those with one.†

## Practical Applications

The practical and clinical applications of our studies and findings have been spelled out in detail in two papers already published.[6,7] In briefest summary, our findings point to the extreme desirability of deciding, with as little diagnostic delay as possible, on the sex of assignment and rearing when a hermaphroditic baby is born. Thereafter, uncompromising adherence to the decision is desirable. The chromosomal sex should not be the ultimate criterion, nor should the gonadal sex. By contrast, a great deal of emphasis should be placed on the morphology of the external genitals and the ease with which these organs can be surgically reconstructed to be consistent with the assigned sex. In cases of female hyperadrenocorticism, good surgical feminization is possible almost without exception, and these patients can, of course, also be hormonally regulated as females when treated with cortisone. Other surgical considerations being equal, the earlier surgical reconstruction of the genitals is done, the better. When operations must necessarily be delayed until later childhood or adolescence, it is sound psychologic medicine to take children into one's confidence and explain the whys and wherefores of what is planned on their behalf. Clitoral amputation in patients living as girls does not, so far as our evidence goes, destroy erotic sensitivity and responsiveness, provided the vagina is well developed. If clitoridectomy is performed in early infancy, the chances of undesirable psychologic sequelae are negligible.

## Theoretical Considerations

Theoretically, our findings indicate that neither a purely hereditary nor a purely environmental doctrine of the origins of gender role and orientation—of psychologic sex—is adequate. On the one hand, it is evident that gender role and orientation is not determined in some automatic, innate, or instinctive fashion by physical, bodily agents, like chromosomes, gonadal structures, or hormones. On the other hand, it is also evident that the sex of assignment and rearing does not automatically and mechanistically determine the gender role and ori-

† In actual fact, the incidence of psychologic nonhealthiness among our 105 patients was surprisingly rare; frank psychosis was entirely absent, except for one instance of schizophrenia of long duration.

entation: The small group of five patients whose sexual outlook diverged somewhat from that of the sex to which they had been assigned prevents so simple-minded a view of environmental determinism. Rather, it appears that a person's gender role and orientation becomes established, beginning at a very early age, as that person becomes acquainted with and deciphers a continous multiplicity of signs that point in the direction of his being a boy, or her being a girl. These signs range all the way from nouns and pronouns differentiating gender to modes of behavior, hair cut, dress, and personal adornment that are differentiated according to sex. The most emphatic sign of all is, of course, the appearance of the genital organs. Presumably, it is the very ambiguity of the external genitals that makes hermaphrodites so adaptable to assignment in either sex, though it requires to be emphasized that the less ambiguous our patients could be made to appear as a result of well-timed plastic surgery and hormonal therapy, consistent with their rearing, the sturdier was their psychologic healthiness.

The salient variable in the establishment of a person's gender role and orientation is neither hereditary nor environmental, in any purist sense of those terms, but is his own decipherment and interpretation of a plurality of signs, some of which may be considered hereditary or constitutional, others environmental. His decipherment of social and environmental signs, whether under the impact of deliberate training and inculcation or through the more casual and haphazard lessons of experience, appears to be markedly more significant than has traditionally been allowed in medical and scientific theories.

Establishment of one's gender role and orientation appears to have much in common with establishment of one's native language. Bilingualism may be native. So also may a gender role and orientation be ambivalent. A native language eventually becomes ineradicable. So also does a gender role and orientation.

Ineradicability of psychologic functions established after birth is seldom given credence in most psychologic theory. There are many medical analogies, however. Bone development, for example, can be effectively influenced in rickets and cretinism only before maturity is reached. Thereafter, deformities of bone growth associated with these diseases become ineradicable.

There are some recent findings in animal psychology that give credence to the viewpoint that psychologic functions, such as gender role and orientation, may become so ineradicable as to appear innately instinctive. We refer to the investigations of Dr. Konrad Lorenz, in Austria, and with one of his examples we shall close.[8] Guided by his own exemplary reasoning, Lorenz experimented and discovered that wild mallard ducklings, immediately upon being hatched, could be induced to react to him as if he were their mother. In contrast with graylag goslings, which unquestioningly accept the first living thing they meet as mother, the mallard ducklings were panicky until they heard the quacking noise usually made by the mother mallard duck. Lorenz imitated the quacking of a mallard mother for half a day, almost continuously, waddling about in a squatting position, lest his height-width ratio produce a visual configuration that dispersed the ducklings in terror. After quacking and waddling with the newly hatched creatures for the first half-day of their lives, Lorenz became established for them as mother. The truly amazing sequel, however, is that the ducklings responded to Lorenz as if he were their mother from that day onward. They trailed behind him on his local excursions, and from the sky or the fields they came flying or running at the sound of the mallard notes he imitated.

## Summary

Over a period of five years, we have made a comprehensive psychologic study of over 100 patients born with divers varieties

of hermaphroditism. With rare exceptions, it was found that the sexual psychology of these patients—their gender role and orientation—was consistent with their sex of assignment and rearing, even when the latter contradicted chromosomal sex, gonadal sex, hormonal sex, the predominant internal accessory reproductive structures, and the external genital morphology. Though the sex of rearing could transcend external genital morphology in psychologic importance, absence or correction of ambiguous genital appearance was psychologically beneficial. Reassignment of the sex of rearing after the early months of life was, without doubt, psychologically injurious.

The Johns Hopkins Hospital.

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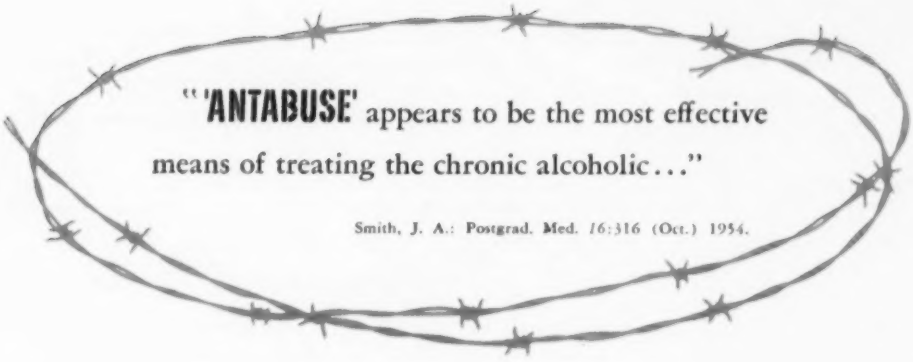


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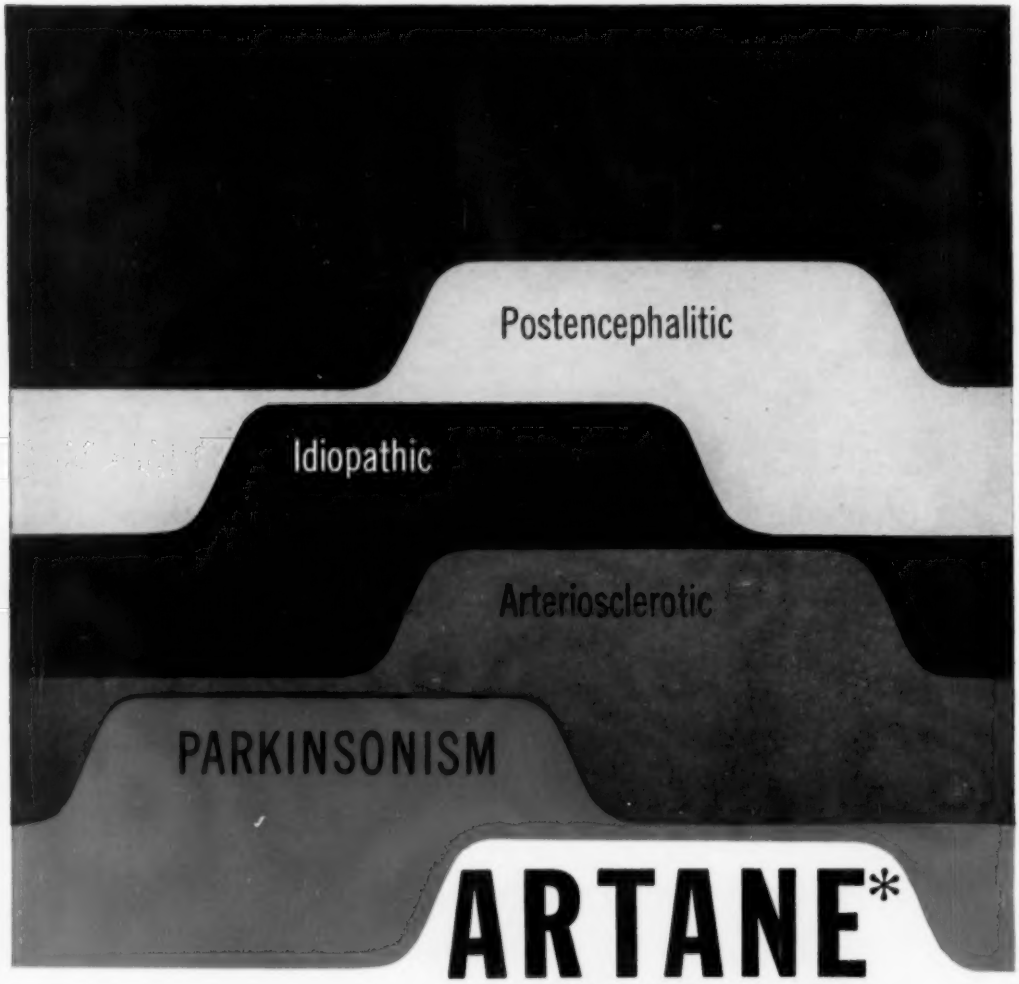


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